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# Helicobacter pylori Virulence Marker from an Area of High

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# Abstracts

## ESOPHAGUS

1

### Exclusion of the Meal Period Does Not Improve the Diagnostic Accuracy of 48-Hour Ambulatory Catheter-Free Esophageal pH Testing

Stephanie L. Hansel, MD, John K. DiBaise, MD\*, Isaac Malagon, BS, Marie Haywood, BSN, Jeannie Stoa, BSN, Virender K. Sharma, MD, H. Jae Kim, MD, Michael D. Crowell, PhD. *Gastroenterology, Mayo Clinic Arizona, Scottsdale, AZ.*

**Purpose:** On the basis of results from small studies using conventional ambulatory catheter-based esophageal pH testing, it has been suggested that exclusion of the meal periods from the analysis is important to ensure optimal diagnostic accuracy. Our aim was to evaluate the results of 48-hour ambulatory catheter-free pH testing depending upon whether the meal period was included or not and determine whether this affected the test's diagnostic accuracy.

**Methods:** 48-hour ambulatory catheter-free esophageal pH tests were analyzed both with the meal period included and excluded in consecutive patients. The patients were divided into two groups based upon whether they were studied on or off PPI therapy. pH parameters evaluated included the total% acid exposure time (AET), total # episodes and Demeester score for day 1, day 2 and the total duration of study. The paired t-test was used to compare pH parameters with meals to without meals. Agreement of final results was also evaluated using the following definitions of an abnormal study: total AET > 5.3%, supine AET > 6.3% or upright AET > 6.7%. A *P*-value < 0.05 was considered statistically significant.

**Results:** 103 patients were studied (56 on PPI, 47 off PPI; 60 female; mean age 60 ± 17 yrs). The most common indications for testing were GERD and unexplained chest pain. There were no significant differences in total AET or Demeester score whether meals were included or not. In contrast, there was a difference in total # episodes with significantly more occurring when meals were included. Nevertheless, there was excellent agreement in terms of final diagnosis for total (95–100%), supine (100%) and upright (96–98%) AET. Identical findings were found for both groups studied (i.e., on PPI and off PPI) and when day 1, day 2 or the full 48 hours were evaluated.

**Conclusion:** Exclusion of the meal period does not improve the diagnostic accuracy of 48-hour ambulatory catheter-free esophageal pH testing.

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### Ethnic Variation in Lower Esophageal Sphincter Pressure and Length

Kenneth J. Vega, MD, M. Mazen Jamal, MD\*. *Division of Gastroenterology, University of Florida/Jacksonville, Jacksonville, FL and Division of Gastroenterology, Veterans Affairs Medical Center, Long Beach, CA.*

**Purpose:** Esophageal manometry (EM) is the gold standard examination for diagnosis of esophageal motor disorders. Normal values for EM in ethnic groups residing in the United States are only available for Hispanic Americans in the literature. The aim of this study was to obtain values of EM in healthy adult African American (AA) volunteers and compare these to those obtained in healthy non-Hispanic white (nHw) volunteers to determine if ethnic variation exists in normal esophageal motor function.

**Methods:** Healthy AA and nHw were recruited from the Jacksonville metropolitan area. Ethnicity was self-reported. Exclusion criteria were symptoms suggestive of esophageal disease, medication use or concurrent illness

that could affect EM. All underwent EM using a solid-state system with wet swallows (Polygram Net, Medtronic Inc., Minneapolis, MN). Resting lower esophageal sphincter pressure and lower esophageal sphincter length were measured at end-expiration while percent peristaltic contractions, distal esophageal contraction velocity, amplitude and duration were measured after 5 cc H<sub>2</sub>O swallows.

**Results:** Fifty-six AA and 48 nHw were enrolled. All subjects completed EM without difficulty. Volunteer age ranged from 18 to 57 years old and was not different between groups. Males comprised 48% of both groups. Resting lower esophageal sphincter pressure, lower esophageal sphincter length and distal esophageal contraction duration were significantly higher in AA than nHw (*P* < 0.05, table). There were no differences seen in percent peristaltic contractions, distal esophageal contraction amplitude, and distal esophageal contraction velocity.

**Conclusion:** Significant ethnic differences exist in EM findings. These differences underscore the need for race specific reference values for EM studies to allow for the accurate diagnosis of esophageal motility disorders in AA patients.

Esophageal manometry parameters in healthy African Americans (N = 56) and non-Hispanic whites (N = 48)

Esophageal manometry parameter	AA (mean ± SD)	nHw (mean ± SD)	<i>P</i> value
Resting LES pressure (mmHg)	32.3 ± 13.9	27.1 ± 9.6	0.03
LES length (cm)	3.66 ± 0.85	3.32 ± 0.83	0.04
% peristaltic contraction	95.1 ± 4.9	94.1 ± 5.9	NS
Distal esophageal contraction amplitude (mm Hg)	97.2 ± 43.8	85.7 ± 31.2	NS
Distal esophageal contraction velocity (cm/sec)	3.59 ± 2.5	4.73 ± 3.49	NS
Distal esophageal contraction duration (sec)	4.45 ± 1.75	3.82 ± 1.26	0.04

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### Nocturnal Gastric Acidity and Nocturnal Esophageal Acidity Are Lower with Immediate-Release Omeprazole Than with Lansoprazole or Esomeprazole in GERD Patients Treated with a Proton Pump Inhibitor

Jerry D. Gardner, MD\*. *Santarus Clinical Research Group. Science for Organizations, Inc., Mill Valley, CA and Santarus, Inc., San Diego, CA.*

**Purpose:** Nocturnal esophageal acidity is particularly important in the pathophysiology of GERD and proton pump inhibitors (PPIs) reduce nocturnal esophageal acidity by reducing nocturnal gastric acidity. Often, comparing mean or median values for gastric or esophageal acidity with one PPI to corresponding values with another PPI may obscure important differences between effects of the two agents on acidity. Our aim was to use Bayesian analyses to compare the relative abilities of immediate-release omeprazole (IR-OME), lansoprazole (LAN), and esomeprazole (ESO) to decrease nocturnal gastric and nocturnal esophageal acidity in GERD patients.

**Methods:** Gastric and esophageal pH were measured for 24 hours in 49 GERD patients on the 7th day of dosing with 40 mg IR-OME, 30 mg LAN or 40 mg ESO in a 3-way crossover study with at least a 10-day washout period between each treatment. Dosing occurred at 10 PM and the nocturnal period was from 10 PM until 6 AM the next morning. Nocturnal acidity was calculated both as integrated acidity (mmol.hr/L) and as time pH < 4 (%).

We used Bayes' rule, which provides a useful method for combining new information with a prior probability, to calculate the posterior probability that nocturnal gastric or esophageal acidity with IR-OME was lower than that with ESO or LAN. For these calculations we used a flat prior probability that considered all values from 0 to 1.00 to be equally probable.

**Results:** The table below shows that with integrated acidity, the posterior probability that nocturnal gastric and esophageal acidity are lower with IR-OME than with ESO or LAN is at least 0.96. With time pH < 4, the posterior probabilities that IR-OME < LAN were the same as those with integrated acidity. On the other hand, with time pH < 4, the posterior probabilities that IR-OME < ESO were the lower than those with integrated acidity.

**Conclusion:** Thus, in GERD patients treated with a PPI, there is a high probability that during the nocturnal period, both gastric and esophageal acidity will be lower with IR-OME than with ESO or LAN.

Posterior Probabilities of Lower Nocturnal Acidity with IR-OME

Measure	IR-OME < LAN		IR-OME < ESO	
	Gastric Acidity	Esoph. Acidity	Gastric Acidity	Esoph. Acidity
Integrat. Acidity	1.00	0.98	1.00	0.96
Time pH < 4	1.00	0.98	0.61	0.80

#### 4

##### Ineffective Esophageal Motility (IEM) and Prolonged Nocturnal Gastroesophageal Acid Reflux

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**Purpose:** To find out whether prolonged (>5 minutes) nocturnal gastroesophageal acid reflux is more prevalent in patients with IEM

**Methods:** We conducted a retrospective database review of esophageal manometry and 24 hour pH studies of patients with esophageal and/or GERD symptoms evaluated at our University Medical Center. We analyzed database from June 2003 to May 2006 and among 400 records reviewed 187 met the study criteria and considered eligible for this analysis. Prolonged nocturnal gastroesophageal acid reflux was defined as a distal esophageal pH < 4 for more than 5 minutes recorded on the ambulatory pH monitor between the hours of 10 pm and 6 am. IEM was defined as low (<30 mm Hg) amplitude or non-transmitted contractions in ≥30% of 10 wet swallows in the distal esophagus.

All patients irrespective of age over 18 years, sex and any racial background that had esophageal manometry and 24 hour esophageal pH study were included in the study. A comparison was made between groups with IEM and normal manometry with respect to the prevalence of prolonged distal esophageal acid exposure between the hours of 10 pm and 6 am.

**Results:** We found that 163 patients had normal esophageal manometry and out of them 84 patients (51.53%) had prolonged nocturnal distal esophageal acid reflux. On other hand, 24 patients had ineffective esophageal motility and out of them 16 patients (66.66%) had prolonged nocturnal distal esophageal acid reflux. Although the frequency of prolonged nocturnal distal esophageal acid reflux appeared higher in patients with IEM as compared to patients with normal esophageal motility, this difference did not reach statistical significance ( $P = 0.16$ ).

**Conclusion:** This study clearly shows that prolonged nocturnal gastroesophageal acid reflux can be present in patients with normal esophageal motility as well as in patients with ineffective esophageal motility. Our study did not show any significant difference in the prevalence of prolonged nocturnal gastroesophageal acid reflux in patients with and without ineffective esophageal motility. By analyzing the data from this cohort of patients, we can conclude that IEM does not play a very significant role in causing prolonged nocturnal gastroesophageal acid reflux. There may be other factors which could be responsible for prolonged nocturnal GERD.

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##### Photodynamic Therapy Decreases DNA Content Abnormalities in Residual Non-Dysplastic Barrett's Esophagus

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**Purpose:** Photodynamic therapy (PDT) has been used for the treatment of Barrett's esophagus (BE) with high grade dysplasia (HGD) or early adenocarcinoma (AC). After PDT, some patients still have residual surface BE (SBE) and/or buried BE (BBE) underlying neosquamous epithelium. The neoplastic potential of residual SBE and BBE post-PDT is unknown.

**Methods:** 52 BE patients with HGD or early AC were treated with PDT. Pre-PDT and post-PDT biopsies were performed. 22 matched pre- and post-PDT non-dysplastic BE samples were retrieved from 11 patients for high fidelity DNA histogram analysis. DNA content changes were compared between pre-PDT SBE, post-PDT SBE and BBE samples. DNA index > 1.1 was considered aneuploid.

**Results:** Of the 11 pre-PDT SBE samples, 3 were diploid and 8 were aneuploid (Table 1). In the 3 patients with pre-PDT SBE diploidy, the post-PDT residual SBE and BBE samples were also diploid. Interestingly, in the 8 patients with pre-PDT SBE aneuploidy, all the post-PDT BBE and 5 post-PDT SBE samples were diploid; 2 post-PDT SBE samples remained aneuploid, and 1 was not analyzed because of insufficient tissue.

**Conclusion:** Compared to pre-PDT BE, post-PDT BE shows significantly less frequent DNA content abnormalities, suggesting that PDT may have a preferential destructive effect on aneuploid cells. This indicates that the post-PDT residual BE, both surface and buried, may have a lower neoplastic potential than pre-PDT BE.

DNA content changes in non-dysplastic Barrett's esophagus before and after photodynamic therapy

Case	Pre-PDT SBE DI	Post-PDT SBE DI	Post-PDT BBE DI
Case 1	1.08	1.06	1.06
Case 2	1.08	1.03	0.98
Case 3	1.03	NP	1.02
Case 4	1.20	1.00	1.05
Case 5	1.27	1.07	1.08
Case 6	1.26	0.93	1.02
Case 7	1.27	NP	1.09
Case 8	1.20	1.06	0.99
Case 9	1.11	1.22	1.08
Case 10	1.25	1.14	0.98
Case 11	1.36	0.98	0.99
Mean ± SD	1.19 ± 0.10	1.05 ± 0.09	1.05 ± 0.04

PDT = photodynamic therapy SBE = surface Barrett's esophagus BBE = buried Barrett's esophagus DI = DNA index NP = not performed

#### 6

##### The Basic Factor in the Genesis of GERD

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**Purpose:** One of the main aims of surgical treatment of gastroesophageal reflux disease (GERD) is a gastropexy restoring the acute angle of His (AH). Most studies attribute GERD to some incompetence of the cardia, deficient esophageal clearing, delayed gastric emptying and transient relaxation of the lower esophageal sphincter (LES).

In the fifties and the sixties, primary importance was attributed to whether AH was acute, preventing the reflux, or obtuse, facilitating and predisposing to this recurrent regurgitation.



Several studies have noted the interaction of multiple factors: gastric acid secretion, hormonal effects, and abnormality in the motility of the cardioesophageal junction (CEJ).

The anatomic aspect of the AH has been bypassed and, in multiple studies, ignored.

While endoscopy may expose the reflux without delimiting the complete aspect of the AH, it is more accurate to add an x-ray study of the upper G.I. tract in order to set the anatomic shape of the CEJ and mainly the AH, which is very variable from person to person.

As we become immersed in the controlling effect of H2 blockers and PPI, we have to debate the correction of an abnormal AH to cure completely some chronic cases of GERD. The anatomic aspect of the AH is a major factor in the competence of the LES, in the motility of the lower esophagus, and in esophageal slurring. It is prominent in the pathogenesis of GERD, and has to be evaluated by X-ray and endoscopy in the management of gastroesophageal reflux.

Is there any explanation of this complete disregard of the importance of AH in the pathology and treatment of GERD? at every gastroenterology meeting, whether national or international, the pharmaceutical industry sponsors large symposia on the subject, to evaluate only the effect of their various proposed drugs in the treatment of GERD, insisting on a long maintenance therapy, which could go on forever?

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#### Double Aortic Arch and Nasogastric Tubes: A Fatal Combination

Julia Massaad, MD, Kelly Crawford, MD\*. Division of Digestive Diseases, Emory University, Atlanta, GA.

**Purpose:** A 38 year old patient was transferred to our hospital for the management of tricuspid valve endocarditis. She had a history of intravenous drug use and had been treated for 2 weeks with intravenous antibiotics but eventually required valvular replacement. On post operative day 11, she developed a massive upper gastrointestinal bleed. An urgent endoscopy showed a large esophageal ulcer with a probable visible vessel at 22 cm from the gums. Endoscopic therapy with epinephrine injections was performed. Two hours later, she bled again, now more severely with secondary shock. Given the location of the esophageal ulcer and the degree of bleeding, a clinical diagnosis of aorto-esophageal fistula was made and the patient was taken to the operating room where an aortic endograft was done with control of the bleeding. On review of her records, it was noted that the patient had a double aortic arch completely encasing her trachea and esophagus on a previous CT of her chest. The patient had an NG tube for more than 5 days post op for feeding and medication administration.

**Discussion:** Double aortic arch is a complete vascular ring that encircles both the trachea and the esophagus. The most common presenting symptoms, usually in the pediatric population, are respiratory and gastrointestinal. The incidence of aorto-esophageal fistula development in adult patients with double aortic arch and prolonged NG intubation has been reported in the literature, and the pathogenesis of this life threatening complication is probably related to the continuous and pulsatile pressure between the aorta and the esophagus. In this anomaly, the trachea and the esophagus are tightly constricted within a double aortic arch and any inserted tubes can produce pressure necrosis and a resultant fistula. Aorto-esophageal fistula is a life threatening complication and its diagnosis can often be delayed in the adult patient without any history of thoracic aortic aneurysms or esophageal malignancy. All imaging modalities to diagnose this entity can be unsuccessful and the best chance for patient survival is a clinical diagnosis made with confidence. We present this case to alert the clinician to another potential and life threatening complication of prolonged nasogastric intubation in this specific patient population.

In conclusion, aorto-esophageal fistula is a highly fatal but potentially avoidable complication in patients with vascular rings and the risks of prolonged nasogastric intubation in this patient population definitely outweighs the benefits.

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#### Prevalence of Esophageal Dysmotility in a Cohort of Patients with Biopsy Proven Eosinophilic Esophagitis. A Prospective Study

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Gastroenterology, Walter Reed Army Medical Center, Washington, DC and Hepatic and Gastrointestinal Pathology, Armed Forces Institute of Pathology, Washington, DC.

**Purpose:** Eosinophilic esophagitis (EE) is increasingly being diagnosed in adults presenting with dysphagia, food impactions and chest pain. EE is best characterized by a dense eosinophilic infiltration of the esophageal epithelial cells. Studies to date provide conflicting data on the association of EE and esophageal dysmotility.

In this study, we intend to evaluate the prevalence of esophageal dysmotility in a cohort of patients with biopsy proven eosinophilic esophagitis (EE) at Walter Reed Army Medical Center. We would hypothesize that esophageal dysmotility is an under recognized feature of EE which may contribute to dysphagia and food impactions.

**Methods:** This study is a prospective evaluation of consecutively identified patients who were diagnosed with EE from 1 March 2005 to present. We intend to enroll up to 32 patients in this study. Those enrolled have had the esophageal biopsies obtained within one year of their inclusion in the study. These patients had not taken swallowed steroids or leukotriene inhibitors for a 6 week period prior to inclusion in the study. All patients were asked to complete a symptom survey that inquired about difficulty swallowing, heartburn, belching, chest pain, regurgitation and waking at night with symptoms. The patients then had esophageal manometry performed to determine the prevalence of esophageal dysmotility.

**Results:** To date, 21 patients (16/21 76% male, Mean {SD} age  $43 \pm 9$  years) have completed the study. In the survey, 18/21 (86%) reported dysphagia, 15/21 (71%) reported heartburn, 8/21 (38%) reported belching, 11/21 (52%) reported chest pain, 14/21 (67%) reported regurgitation, 9/21 (42%) reported waking at night with symptoms. All patients were found to have a normal lower esophageal sphincter pressure ( $12 \pm 5$  mm/Hg). Of the 21 patients, 3 (14.2%), (95% CI 3.1%, 36.3%) were diagnosed with a non-specific esophageal motor disorder compared to a prevalence of 10% in a population of patients with GERD,  $P = 0.351$  using the binomial test.

**Conclusion:** This is preliminary data, but, suggests that the prevalence of a non-specific esophageal motor disorder in EE patients is similar to that in patients with GERD.

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#### Rabeprazole Sodium 20 mg BID Improves Symptoms in Patients with Chronic Persistent Asthma

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**Purpose:** Prior studies have demonstrated a potential benefit of PPI's for the treatment of chronic persistent asthma (CPA) in patients with underlying GERD. Mechanisms may include reduced microaspiration or inhibition of vagally-mediated airway bronchoconstriction. Our purpose was to determine whether rabeprazole sodium delayed-release tablets (Aciphex®) at double dose was efficacious in improving objective and subjective measures of pulmonary function in patients with CPA.

**Methods:** Patients with concomitant GERD and CPA were treated for 3 months with Aciphex® 20 mg BID after a 2 week titration off their usual PPI or H2RA. At baseline, 1 month, and 3 months patients completed the validated Quality of Life in Reflux and Dyspepsia (QOLRAD) and Asthma Quality of Life Questionnaire (AQLQ) surveys. Patients underwent peak flow measurement at baseline and at the conclusion of the study.

**Results:** We recruited 39 females, 9 males. Mean age  $48.2 \pm 1.6$ . Overall 26 (54.2%) patients were on inhaled corticosteroids, 10 (20.8%) were on a leukotriene receptor antagonist, and 42 (87.5%) were on a short or

long-acting  $\beta$ -agonist. None were on oral steroids. All 48 patients completed the 3 month study and remained compliant with Aciphex® therapy. AQLQ scores improved at month 1 by 40.7 points ( $P < 0.001$ ) and continued to improve at month 3 (43.1 points from baseline,  $P < 0.001$ ). Likewise peak flow values improved significantly from baseline (285 ml) to the assessment at month 3 (323 ml;  $P = 0.008$ ). GERD symptoms were reduced to nearly half during the study period as well (QOLRAD baseline = 89.9 to month 3 = 47.3;  $P < 0.001$ ). Improvements in AQLQ, QOLRAD, and peak flow during Aciphex® treatment remained significant even after adjustment for age, BMI, gender, and asthma treatment regimen. There was good correlation between improvement in the AQLQ and QOLRAD ( $r = 0.71$ ;  $P < 0.001$ ). No patient required hospitalization, oral steroids, or additional medical therapy for CPA during the study period.

**Conclusion:** Our data supports the published literature that potent acid suppression in patients with CPA can improve respiratory symptoms. Objective improvement in FEV1 as measured by peak flow correlated with subjective assessment of improvement. Improvement was independent of patient characteristics such as age, gender, and BMI. Improvement was similar in patients on or off inhaled steroids,  $\beta$ -agonists, or leukotriene receptor antagonists. Our study should be replicated in a larger group using a double-blinded therapeutic trial design.

## 10

## A Case of Severe Heartburn

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**Purpose:** A 64 yo white male with a history of recurrent paroxysmal atrial fibrillation was admitted to the hospital for elective surgery. He had failed multiple conventional therapies including anti-arrhythmic agents and two previous ablations, but continued to be symptomatic. He was deemed a candidate for minimally invasive pulmonary vein ablation with left atrial appendage ligation, or the mini-MAZE procedure.

He underwent the mini-MAZE procedure and tolerated the procedure well. His post-operative course was complicated by weakness, inability to ambulate and recurrent atrial arrhythmias requiring continued anticoagulation. By POD day #5, he began to complain of anorexia, nausea and abdominal discomfort. A preliminary work-up included normal liver and pancreatic enzymes, abdominal ultrasound and CT scan. Despite this, his WBC count continued to rise to approximately 18,000. On POD Day #10, the patient developed four episodes of melena. His anticoagulation was discontinued and GI was consulted.

Upon questioning, the patient described dysphagia, epigastric fullness and anorexia. His history included a duodenal ulcer at age 15. Physical exam revealed a well-appearing male with a normal abdominal exam. He was noted to be tachycardic with a heart rate of 104. The patient was placed on an esomeprazole infusion and the decision was made to proceed with an EGD to evaluate upper GI bleeding.

EGD revealed what appeared to be a full thickness burn and necrosis at 25–30 cm from the incisors with formation of a pseudodiverticulum. The findings were suspicious for a contained perforation, likely related to the radiofrequency ablation 11 days prior. An emergent CT scan was obtained which revealed a small mediastinal space tract that appeared to connect to an esophageal defect. There was no evidence of free air in the mediastinum to suggest an ongoing leak.

The patient was taken emergently to surgery and findings included the above mentioned anterior full-thickness perforation of the esophagus that extended for approximately 2 cms. The patient underwent flexible esophagogastroscope, placement of esophageal drainage mesogastric tube, exploratory laparotomy, feeding jejunostomy and Stamm gastostomy placement. The esophageal perforation was followed with periodic EGDs and gastrografin swallow studies. He began tolerating a soft diet and was eventually discharged to a rehabilitation facility 50 days after the initial mini-MAZE procedure.

In conclusion, there needs to be a high index of suspicion for esophageal perforation after the mini-MAZE procedure.

## 11

## Proton Pump Inhibitor and Nonsteroidal Anti-Inflammatory Use and the Development of Neoplasia in Barrett's Esophagus

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**Purpose:** The role of chemoprevention in Barrett's esophagus (BE) is unclear. Evidence suggests a protective role for proton pump inhibitors (PPIs), non-steroidal anti-inflammatories (NSAIDs), and possibly statins. However, human data are limited.

**Methods:** This is a retrospective study of a well characterized large cohort of patients with documented BE diagnosed between 1985 and 2005. Prescription information was collected from pharmacy records before and after BE diagnosis. Patients were followed until the development of dysplasia, adenocarcinoma, death, or 12/2005. Cox regression analyses were performed to examine the association between NSAID, PPI, or statin prescription and the risk of developing dysplasia or cancer.

**Results:** We examined 408 patients with BE with a mean age of 61 at the time of BE diagnosis; Caucasian 91.2%, men 94.4%. The mean duration of follow-up was 6.6 years (SD 4.9). During 2690 patient-year follow-up, 125 developed dysplasia (20 high grade) yielding an incidence of 4.65 per 100 PY and 29 patients developed adenocarcinoma (1.08 per 100 PY). Approximately 38.4% were prescribed NSAIDs for a mean duration of 12.9 months, 66.4% were prescribed a PPI for a mean duration of 31.5 months, and 26.2% were prescribed a statin for a mean duration of 10.5 months.

In unadjusted analyses, only patients with BE segment > 3 cm, and more recent time of BE diagnosis were associated with increased risk of dysplasia or cancer, whereas PPI prescription was associated with reduction in that risk. This persisted in multivariable analysis (Table), and were exaggerated in analysis limited to those developing dysplasia or cancer after the first year of diagnosis; for example, PPI use (0.23, 95% CI: 0.10–0.61). No consistent associations were observed for NSAID or statin use where neither any prescription nor prescriptions > 12 months was associated with the risk of dysplasia or cancer.

**Conclusion:** PPI use seems to reduce the risk of neoplastic changes in patients with BE. NSAID or statin use is not associated with the risk of neoplasia.

Multivariable COX Ph model predicting the risk of dysplasia

	Hazard Ratio	95% CI
Non-Caucasian	0.51	0.24–1.10
BE length > 3 cm	1.53	1.01–2.29
PPI prescription	0.64	0.43–0.94

## 12

## Measurement of Lower Esophageal Sphincter (LES) Characteristics during Esophageal Manometry Does Not Differ with Severity of Ineffective Esophageal Motility

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**Purpose:** Manometric assessment of Lower Esophageal Sphincter (LES) includes Resting Pressure and LES relaxation characteristics (Residual

Pressure) with liquid and viscous swallows. LES pressures are not traditionally used to establish the severity of IEM.

**Aim:** To determine whether LES pressures vary with severity of IEM

**Methods:** Retrospective review of 180 MII-EM studies done in patients diagnosed with IEM by "Old" (presence of  $\geq 30\%$  liquid swallows with contraction amplitude  $< 30$  mm hg in the distal esophagus) or "New" (presence of  $\geq 50\%$  of ineffective liquid swallows) criteria for IEM. IEM classified as mild (normal bolus transit for both liquid and viscous), moderate (bolus transit only for liquid or viscous), or severe (abnormal bolus transit for both liquid and viscous).

Means of LES resting pressure, LES liquid residual pressure and LES viscous residual pressure were calculated and compared among Mild, Moderate and Severe groups by ANOVA.

**Results:** Mean LES resting pressure was higher only for mild versus moderate IEM by the "New" IEM criteria. All other comparisons showed no difference in LES resting pressure. Additionally, there was no difference in LES residual pressures in both "Old" and "New" criteria.

**Conclusion:** Our findings suggest that LES characteristics are overall very similar across IEM of different severity, independent of the criteria used.

"Old" IEM Criteria			
"Old" IEM	Mean LES Resting Pressure	Mean LES Liquid Residual Pressure	Mean LES Viscous Residual Pressure
Mild	21.8	4.7	4.4
Moderate	21.5	4.8	5.4
Severe	26.4	4.9	5.1

"New" IEM			
"New" IEM	Mean LES Resting Pressure	Mean LES Liquid Residual Pressure	Mean LES Viscous Residual Pressure
Mild	19.2*	3.0	4.5
Moderate	26.0*	3.6	4.1
Severe	20.5	2.6	3.2

\* $P < 0.05$

### 13

#### Eosinophilic Esophagitis: A Common Cause of Food Impaction and Dysphagia in Young Men

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**Purpose:** Eosinophilic Esophagitis (EE) is an increasingly recognized condition in adults characterized by esophageal mucosal eosinophilia in the setting of dysphagia or food impaction. We undertook a retrospective review of all cases seen in our Gastroenterology Clinic to evaluate for demographic information including gender predilection, presenting symptoms including dysphagia score, associated conditions, endoscopic and histologic appearance and response to treatment.

**Methods:** A retrospective review of medical records from January 2003 to August 2006 was completed. Data was analyzed by calculating means with standard deviations for continuous variables and percentages for categorical variables. Dysphagia scores were assessed based on presenting history and reassessed based on further progress notes when available. Statistical calculations were completed with the aid of SAS software.

**Results:** Twenty-five patients were identified. Age at presentation was  $26.1 \pm 6.4$  years. Age at symptom onset was  $23.8 \pm 7.8$  years. 94% of patients were male. 96% of patients presented with solid dysphagia or food bolus impaction. 92% of patients had either concentric rings or linear furrows

reported on initial endoscopy. Biopsy revealed  $47 \pm 40$  eos/hpf (range 26–200). 22% of patients also were asthmatic and 55% of patients had a history of asthma, atopy and/or a positive allergy skin test. Patients were treated with a variety of modalities including dilation, PPI's, food avoidance and swallowed fluticasone. Patients had significantly less dysphagia after treatment (median score 2.4 prior to treatment and 0.7 after treatment,  $P < 0.01$ ) and there was no trend favoring a specific treatment. There were no perforations or significant complications from dilation.

**Conclusion:** EE is a recently recognized disease of increasing frequency. Early recognition and treatment of EE could prevent food impaction and the risk of mucosal tears with treatment. One should suspect EE in younger men with solid dysphagia and any history of allergic disease. EE appears responsive to a variety of therapies. Dilation appeared safe in our series in contrast to prior series that showed substantial perforation rates. Potential areas for further study include prospective trials of specific treatment modalities and symptom recurrence after intervention.

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#### GERD, Helicobacter Pylori and MGUS – Is There a Relationship?

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**Purpose:** Monoclonal Gammopathy of unknown significance is characterized by low levels of monoclonal protein (M protein) in the serum or urine that is produced by a single clone of plasma cells. There has been no literature confirming the etiology of this condition. Recently, MGUS has been found to be associated with chronic infections (Hep B, C and HIV) and autoimmune diseases. While making an attempt to recognize additional associated factors, we searched for other chronic inflammatory conditions (example GERD) and other subtle chronic infections (example H. Pylori). There is no literature available on the incidence of GERD in MGUS. Moreover, there has been conflicting reports on the prevalence of H. pylori and MGUS.

**Methods:** We identified 394 patients with MGUS at veterans affairs medical center, Kansas City diagnosed over last 20 years. Charts on these patients were reviewed for clinical diagnosis of GERD, endoscopic findings, pathological biopsies, H. Pylori staining on histology, SPEP/IFE, immunoglobulin levels and bone marrow biopsies.

The control group consisted of randomly selected patients (N = 400) from out patient primary care clinic at the same institution.

**Results:** 41% (162/394) of patients with MGUS were noted to have moderate to severe symptoms of GERD as compared to 25% (102/400) in the control group. 60% (97/162) of MGUS patients with GERD underwent endoscopies as compared to 41% (42/102) of patients in the control group. Histology was positively stained for H. Pylori in 27.8% patients (27/97) in MGUS and 14% (6/42) of control group. We found no correlation between H pylori positivity and type or level of monoclonal protein in MGUS. In addition, we observed no change in immunoglobulin levels following treatment and eradication of h pylori in MGUS patients

**Conclusion:** At our institution, patients with MGUS have higher prevalence of GERD. Our findings need to be confirmed and verified in further prospective studies. No correlation was seen between H. pylori infection and MGUS.

Patient Characteristics		
Pt characteristics	MGUS(394)	General Pop (400)
Median Age	74	65
GERD	162	102
Endoscopies	97	42
H. Pylori	27	6
BMI	28	28.17

Prevalence of GERD

GERD	MGUS (N = 394)	Control (N = 400)
Present	162	102
Absent	232	298

*P* value < 0.001

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### TAK-390MR vs. Lansoprazole (LAN) for Maintenance of Drug Concentration above a Threshold Which Corresponds to Higher%-Time pH > 4

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**Purpose:** TAK-390MR is a proton pump inhibitor employing modified release (MR) technology designed to provide prolonged plasma concentration of TAK-390 following once daily oral dosing. To better characterize the relationship between drug exposure and%-time intragastric pH > 4, a threshold plasma TAK-390 concentration was identified using modeling. The ability of the MR formulation to keep drug concentration above this threshold was evaluated and compared to that of LAN's delayed-release dosage form.

**Methods:** Post-hoc analysis and modeling was conducted using data from 3 open-label, multiple-dose, single-center, crossover phase 1 studies to determine a threshold plasma concentration and a model that maximizes the relationship between the%-time that intragastric pH > 4 and the%-time that plasma concentrations are above a threshold value over a 24 h postdose interval. LAN (30 mg), TAK-390 (20, 30, 60, 90, or 120 mg), or TAK-390MR (60, 90, or 120 mg) plasma concentrations were measured within 24 h after 5 days of daily dosing. Nine TAK-390 concentration levels (15, 30, 60, 125, 250, 500, 1000, 2000, and 3000 ng/mL) were evaluated as possible thresholds; the %-time that plasma concentrations were above each threshold over 24 h postdose was determined. Four models were used to characterize the relationship between the %-time that plasma concentrations were above a threshold and the %-time pH > 4 during 24 h postdose; AIC was used to identify the *best fitted* model and threshold plasma concentration. The %-time plasma concentrations were above this threshold for LAN and TAK-390MR were assessed.

**Results:** Data from 92 subjects were analyzed. Based on this analysis, 125 ng/mL was derived as the threshold. For LAN (30 mg), the mean %-time that plasma concentrations were > 125 ng/mL was 17%, compared to 34–50% for TAK-390MR regimens (30–120 mg). Based on the *best fitted* model, the mean %-time above the 125 ng/mL threshold for LAN corresponds to an estimated %-time of pH > 4 of 50% compared to 65–70% for TAK-390MR regimens.

**Conclusion:** Based on TAK-390 and LAN data, the plasma concentration of 125 ng/mL was identified as the threshold that maximizes the relationship between the%-time plasma concentration above this level and the%-time intragastric pH > 4 over 24 h postdose. In this analysis, TAK-390MR maintains plasma drug concentrations above this threshold approximately 2–3 times longer than LAN. This difference appears to provide greater %-time pH > 4.

## 16

### Endoscopic Full-Thickness Plication for the Treatment of GERD: Five Year Multi-Center Results

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**Purpose:** We previously reported the Plicator (NDO Surgical, Inc., Mansfield, MA) procedure, which is an endoscopic procedure that delivers a full-thickness plication, to be effective at reducing GERD symptoms and medication use for up to 3-years post-plication with no long-term procedural adverse events. The purpose of this study was to assess the long-term safety and treatment durability of the Plicator up to 5-years post-plication.

**Methods:** Subjects with chronic heartburn who had originally participated in the open-label study and received a single plication in the gastric cardia approximately 1 cm below the gastroesophageal junction were eligible. Subjects were evaluated at baseline for GERD symptoms and medication use. Long-term subject follow-up was completed to evaluate safety and long-term treatment durability.

**Results:** Twenty-eight subjects completed the long-term follow-up (mean follow-up interval: 5 years (58 months), range: 50–65 months). All procedure-related adverse events occurred acutely, as previously reported, and no new adverse events were observed during extended follow-up. At 5-years post-procedure, 62% of baseline PPI-dependent patients remained off daily PPI therapy. Treatment effect remained stable from the 3 to 5-year follow-up interval, with 16/28 patients off daily PPI at 3-years compared to 15/24 patients at 5-years. Median GERD-HRQL scores remained significantly improved at 5-years versus baseline off-meds scores (10 vs. 19, *P* < 0.001). In addition, the proportion of patients achieving ≥ 50% improvement in GERD-HRQL score was consistent from 3-years (55%) to 5-years (50%).

**Conclusion:** Endoscopic full-thickness plication can effectively reduce GERD symptoms and medication use for at least 5-years post-procedure. Treatment effect is stable for 5-years and there are no long-term procedural adverse effects.

## 17

### What Is the Truth? Sleep Disturbance as Assessed by Investigators or a Validated Instrument (ReQuest™) in Patients with GERD

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**Purpose:** Sleep disturbance in GERD patients impairs quality of life and reduces work productivity. Over- and under-reporting of symptoms before, during and after therapeutic intervention is a well-known phenomenon in daily clinical practice. We systematically assessed sleep disturbance in a GERD trial utilizing assessment by the investigator and ReQuest™, a validated sensitive tool for the evaluation of GERD symptoms.

**Methods:** In this open, multinational, multicenter trial 633 GERD patients were treated with pantoprazole 40 mg daily for 28 days. For the assessment of GERD symptoms patients completed ReQuest™ daily, while the investigator assessment was performed at day 0, 14 and 28. The proportion of patients troubled by sleep disturbance on all of the 7 consecutive days prior to day 0, 14 and 28 was compared between patient self-assessment with ReQuest™ and investigator assessment and 95% confidence intervals were calculated.

**Results:** The comparison of point estimates and confidence intervals for the proportion of patients (PP; nequals; 538) yielded a statistically significant difference at baseline, during and after therapy between the two modes of assessment.

**Conclusion:** There is a discrepancy between investigator and patient symptom assessment regarding the proportion of GERD patients with sleep disturbance. The reduction of these numbers over time is similar comparing the two assessment modes. The significantly lower proportion of patients assessed as suffering from sleep disturbance according to investigator assessment may be due to underestimation of symptoms by the investigator. Thus, investigator assessment alone may not be the optimal means to evaluate sleep disturbance (and other symptoms) in GERD patients, as underestimation

of symptoms may lead to inappropriate therapeutic decisions. These data may also suggest that prolonged PPI treatment might be required to properly improve GERD related sleep disturbance.

Proportion of Patients Suffering from Sleep Disturbance (%; CI 95%)		
	ReQuest™ assessment	Investigator assessment
Day 0	84.9% [80.7, 88.5]	53.9% [49.6, 58.2]
Day 14	69.6% [65.4, 73.5]	40.2% [36.0, 44.5]
Day 28	56.9% [52.3, 61.5]	29.0% [25.2, 33.1]

## 18

### Pantoprazole Is Significantly More Effective in Relieving GERD Symptoms Than Esomeprazole

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**Purpose:** Symptom relief is known to be the most important treatment outcome for GERD patients, as symptoms impair the health related quality of life substantially.

**Methods:** Results from a randomised, double blind, multicenter study conducted in Brazil, Germany, Hungary, and Italy are presented. In patients with GERD Grade II/III Savary-Miller (verified by initial endoscopy) the effect of pantoprazole 40 mg once daily (qd) (PANTO) and esomeprazole 40 mg qd (ESO) on GERD symptoms was compared after 28 days of treatment. The investigator documented the intensity of GERD-associated symptoms (heartburn, acid regurgitation, dysphagia, epigastric pain/discomfort, flatulence, retrosternal tightness, fullness, nausea/vomiting, lower abdominal pain, sleeping disturbance, burping/belching, and coughing) described as none (0), mild (1), moderate (2), or severe (3). Freedom from symptoms was defined as the absence of all symptoms for at least 3 days before the visit. Symptom relief was compared between the treatment groups by using the one-sided Median Two-Sample Test.

**Results:** In the per-protocol population 290 patients were included. At baseline, the mean sum scores of GERD-associated symptoms were comparable between the two treatment groups (PANTO: 11.17; ESO: 11.60;  $P > 0.05$ ). After 4 weeks of treatment the mean sum scores decreased significantly to 1.35 in the PANTO and 1.68 in the ESO group ( $P < 0.05$ ), implying symptom relief rates of 56.3% and 46.6%, respectively.

**Conclusion:** After 28 days of treatment more patients were without GERD symptoms with PANTO and their symptom load was significantly more reduced compared to ESO.

## 19

### Black Esophagus Associated with Malignancy and Use of FOLFOX/Avastin

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**Purpose:** Black esophagus is an endoscopic diagnosis characterized by necrotic tissue in the esophagus. It is a rare diagnosis, with less than 100 cases reported in the literature over the past 50 years. Black esophagus has been associated with severe illness and infection, but its association with malignancy or specific chemotherapeutic agents has not been reported. We describe cases of black esophagus at our institution over the past three years, with special attention paid to the presence of malignancy.

**Methods:** We performed a retrospective chart review on all patients that had the endoscopic diagnosis of "black esophagus" or "necrotic esophagus" between 2004 and 2007. We evaluated patients' age, gender, indication for endoscopy, presence of malignancy, pathologic reports, treatment with chemotherapeutic agents and 6 month mortality. We present continuous data as means and categorical data as percentages.

**Results:** Six patients with black esophagus were identified. Half of these patients were female and the mean age was 65 years. The most common indication for endoscopy was hematemesis (83%). Five of our six patients had malignancy: colon (2), small bowel (1), pancreas (1), breast (1), prostate (1). One patient had both colon and prostate cancer. Three patients had received chemotherapy, and two of these (66%) had received FOLFOX (Oxaliplatin, fluorouracil, and leucovorin). The 6 month mortality of patients in our series was 33%.

**Conclusion:** In this small case series, malignancy was highly prevalent among our patients with black esophagus. Of the patients that had recently received a chemotherapeutic agent, the majority had been treated with FOLFOX/avastin. Oxaliplatin and fluorouracil are both known to cause mucositis and fluorouracil can cause esophagitis. The association with the administration of FOLFOX/avastin and the development of black esophagus in this case series should foster consideration of this important outcome in patients receiving this chemotherapeutic regimen.[figure1]

PATIENT	AGE	GENDER	PRESENTATION	MALIGNANCY	CHEMOTHERAPY	OUTCOME
1	62	F	Hematemesis + Melena	Breast	-	Died
2	67	M	Hematemesis	Colon Prostate	-	-
3	44	F	Hematemesis	-	-	-
4	54	M	Emesis	Pancreas	-	-
5	68	F	Hematemesis	Colon	FOLFOX / Avastin	-
6	66	M	Hematemesis	Small Bowel	FOLFOX / Avastin	Died
TOTAL	66	50/50	*****	83% Ca		33%

## 20

### Clinical Efficacy and Problems of a Simple Questionnaire (F-Scale) for the Diagnosis of GERD in the Elderly

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**Purpose:** Gastro-esophageal reflux disease (GERD) is a common disease in Western countries. Recently, the prevalence of GERD is increasing in a Japanese population with a high prevalence of atrophic gastritis. Although it is difficult to diagnose accurately GERD by non-invasive tests, a simple questionnaire (F-scale) to score GERD symptoms is now produced in Japan, which has a good correlation with endoscopic findings. However, it may be difficult for elderly people to understand the questions and to fill out a questionnaire correctly in a short time. The aim of this study was to evaluate the efficacy of F-scale for the diagnosis of GERD symptoms in the elderly.

**Methods:** 1686 consecutive patients (797 men and 889 women with a mean age of 43 years) who first attended the Outpatient Department of General Medicine and Emergency Care of Toho University were enrolled in the present study. They were asked to respond the F-scale questionnaire regardless of their chief complaints. This questionnaire was devised from 12 questions, which were scored to indicate the frequency of symptoms, as follows: never = 0; occasionally = 1; sometimes = 2; often = 3; and always = 4. If the patient has a score of more than 7 point, GERD is considered as positive.

**Results:** A total of 647 patients with GERD were identified. The positive rate of the questionnaire was 277 of 797 men (35%) and 361 of 889 women (41%). Unexpectedly, the prevalence of GERD was highest in the 20–29-aged group (45%), followed by the 30–39-aged group (40%), and the 40–49-aged group (39%). The group aged with 70–79 had the lowest prevalence (26%) and had the largest proportion of patients with a point of zero.

**Conclusion:** The prevalence of GERD symptoms in general practice was much higher than reported previously. Furthermore, the prevalence of GERD was highest in the group aged with 20 to 29 and decreased with age. The lower prevalence in aged persons may reflect the difficulties in filling out F-scale. GERD symptoms are possibly underestimated in the elderly.

## 21

### Long Term Follow up of Patients Treated with Stretta

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**Purpose:** Assess long term durability of Stretta procedure for GERD based on intent to cure criteria.

**Methods:** Telephone and in person interviews were done on 56 of 61 patients who underwent Stretta procedure for GERD from 53 to 60 months previously. The only parameter used to judge long term effectiveness was the use of PPIs, as our intent was to resolve GERD symptoms. Quality of life assessments were not evaluated.

**Results:** Of the 56 patients (92%) available for follow up only 9 (16%) were not using PPI. None of these patients have had post Stretta complaints requiring further evaluations of the esophagus or stomach. Of the 47 patients using PPI, 39 (83%) had 3, 6 and/or 12 month follow up questionnaires that indicated improvement in GERD symptoms, but later needed to resume PPI use. Time to resumption of PPI use in the nonresponders ranged from 0 to 23 months (median 14.6 months). Five patients (10%) developed symptoms of gastroparesis confirmed by nuclear imaging studies. Six patients (13%) required esophageal dilations for dysphagia. One patient in this group had a fundoplication after Stretta. No predictors of a favorable result could be identified based on pre Stretta evaluations with endoscopy, esophageal motility testing or 24 hr pH testing, but the highest DeMeester score in the favorable outcome group was 47.4.

**Conclusion:** The Stretta procedure does not provide durable long term relief for GERD. If the intent of use of the Stretta procedure is to cure GERD symptoms and avoid use of PPIs, only a small percentage of patients can be expected to benefit. A substantial percent of nonresponders require further treatment for dysphagia and gastroparesis

## 22

### Presentation and Prognosis of Esophageal Adenocarcinoma in Patients below Age 50

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**Purpose:** Esophageal adenocarcinoma (EAC) has one of the fastest growing incidence rates of all cancers in the United States. Although the majority of patients are diagnosed at an advanced age, EAC is now increasingly recognized in younger patients in whom the clinicopathologic features have been poorly described.

The aims of this study are to compare clinical presentation between early (i.e.  $\leq 50$  years) and later onset EAC, and to evaluate factors associated with survival.

**Methods:** Records of patients with EAC diagnosed 1994–2004 were retrospectively reviewed. Data were collected on demographics, social history, family history of cancer, clinical presentation, diagnosis during Barrett's surveillance, endoscopic and histologic findings, treatment, and sur-

vival. Chi square analysis was performed for group comparisons. Survival was assessed with Kaplan-Meier analysis and the log-rank test. Cox models were used for multivariable analysis in a stepwise backwards manner.

**Results:** 31 of 242 (12.8%) of EAC patients were  $\leq 50$  years at diagnosis. There was no difference between the two groups in sex distribution, smoking history, family history of cancer, or GERD. Patients  $\leq 50$  years were more likely to present with dysphagia (80% vs. 60%,  $P < 0.002$ ) and have dysphagia for  $> 6$  months (25% vs. 7%,  $P < 0.0001$ ). Patients  $\leq 50$  years were more likely to have lymphatic spread at diagnosis (48% vs 31%,  $P = 0.015$ ). There was no difference in the T or M stage at presentation. Median survival was 16.3 months (13.2–21.4) for younger patients and 22.3 months (16.2–28.4) for older patients ( $P = NS$ ). Factors associated with shortened survival were dysphagia at presentation, advanced histologic grade, lymphatic spread and esophagectomy. By multivariable analysis shortened survival was associated with histologic grade ( $P = 0.03$ ) and lymphatic spread ( $P = 0.01$ ). In 16 patients EAC was detected during Barrett's surveillance, all of whom were older than age 50. There was no survival difference whether or not EAC was diagnosed in a surveillance program.

**Conclusion:** 1) Patients under age 50 comprise a significant minority of newly diagnosed EAC. 2) Diagnosis is delayed in younger patients presenting with dysphagia, thereby contributing to adverse outcomes and advanced stage at time of diagnosis. Early endoscopy should be considered in the evaluation of GERD and dysphagia, particularly for patients younger than 50 years.

## 23

### Prevalence and Impact of Co-Morbid Psychological Distress on Response to PPI Therapy in Patients with GERD

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**Purpose:** Co-morbid psychological distress (PD) has been reported in a substantial proportion of GERD patients (pts). However, little is known about the impact of PD on response to proton pump inhibitor (PPI) therapy.

**Aims:** Determine the prevalence of co-morbid psychological distress and its impact on response to PPI therapy in GERD pts.

**Methods:** Pts undergoing EGD for heartburn  $> 2 \times$ /week were recruited. Pts who had taken a PPI within 2 weeks of EGD were excluded. Participants completed validated questionnaires (DHSI, RDQ, QoLRAD, BSI) and were treated with rabeprazole 20 mg/d  $\times 8$  wks after which follow-up surveys were completed. Pts were categorized as suffering from nonerosive disease (NERD) or erosive disease (EE) at EGD. Psychological distress was defined as a composite BSI score  $> 63$ .

**Results:** 101 pts (67 NERD, 34 EE, female = 54%, mean age = 48 yrs) completed the treatment period and both sets of surveys. 42% of GERD pts had co-morbid PD. There was no difference in the prevalence of PD in NERD vs. EE. Overall, pts reported significant improvements in GERD symptoms and disease specific QoL after rabeprazole ( $P < 0.001$ ). Before PPI therapy, co-morbid PD was associated with greater GERD symptoms and significantly worse disease specific QoL. Following PPI therapy, pts with and without PD experienced similar magnitudes of improvement in GERD symptoms and QoL. However, pts with co-morbid PD had significantly more residual GERD symptoms and worse disease specific QoL after PPI than did those without PD (see table).

**Conclusion:** Over 40% of GERD pts had co-morbid PD. GERD outcomes improved with PPI therapy regardless of the presence or absence of PD. However, pts with PD had more severe baseline GERD symptoms and worse QoL than those without PD. Further, pts with PD were left with more residual symptoms and reduced QoL after PPI therapy. These observations highlight the importance of identifying psychological distress when approaching the treatment of GERD and identify an important subgroup of GERD pts who might mistakenly be labeled as PPI nonresponders.

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Effect of PD on RDQ and QoLRAD

	BSI > 63 (N = 42)	BSI < 63 (N = 59)	P value
RDQ-Before	16.1	13	0.077
After PPI	9.8*	4.9*	0.007
QoLRAD-Before	3.5	4.5	<0.001
After PPI	4.6*	5.4*	0.006

\*Significant improvements after PPI,  $P < 0.001$

## 24

### Yo-Yo Lipoma in My Esophagus

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**Purpose:** Esophageal lipomas are exceedingly rare with only a handful of documented case reports to date. We report a case of a large esophageal lipoma inducing symptoms of gastroesophageal reflux disease (GERD). We herein advocate the utility of esophagostrodeudonoscopia (EGD) and endoscopic ultrasound (EUS) in diagnosing gastric lipomas and aiding in subsequent removal without the need of invasive surgery.

**Case Report:** A 62-year-old female with a three-year history of GERD presents with recurrent heartburn. The patient tried a three-month period of a proton pump inhibitor that was also refractory to symptoms.

The patient was evaluated with an EGD that demonstrated a 2 cm × 2 cm submucosal pedunculated mass extending from a narrow stalk at the distal esophagus (Fig. 1). On endoscopy, the mass was observed slipping in and out of the GE junction like a 'yo-yo' (Fig. 2). An endoscopic ultrasound was then performed demonstrating no vasculature and findings consistent with a lipoma (Fig. 3).

The 2×2 cm mass was then removed using a hot snare and extracted with a Roth basket after passing it in the stomach. The esophagus was left intact without complication (Fig. 4). The pathology demonstrated the tissue to be consistent with a lipoma (Fig. 5). The patient tolerated the procedure well with resolution of her GERD and was discharged home the same day.

**Discussion:** Lipomas can be diagnosed based upon physical appearance, but have low sensitivity. Cushion sign or pillow sign has demonstrated 40% sensitivity and 98.8% specificity. EUS offers a more definitive method for diagnosis of lipomas and according to Hwang et al., can be diagnosed by EUS characteristics alone without need for histopathology. EUS can also assist and aid in mapping the grounds of a tumor, and ruling out possible vasculature invasion of tumors.

Previous case reports and series have used open surgery and laparoscopic means to remove esophageal tumors. However Wehrmann et al. states in their case series that esophageal masses less than 4 cm in size can be safely removed using both EUS and EGD. Our case further corroborates the utility of EUS and EGD in removing esophageal lipomas. It also provides a safer and less invasive alternative than either open or laparoscopic surgery. Furthermore, to the authors' knowledge, this is the first described case of a lipoma inducing GERD with complete resolution of symptoms following lipoma removal utilizing EUS and EGD.

## 25

### Endoscopic Full-Thickness Plication for the Treatment of GERD: 6 Month Data of the German Multi-Center Serial Implant Trial

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**Purpose:** In a recently published prospective randomized, sham-controlled trial, the Plicator™ (NDO Surgical, Inc.) proved effective at controlling reflux symptoms and reducing medication use and esophageal acid exposure. In several cases the narrowing of the GE-junction remains incomplete with a single Plicator implant. Therefore, we evaluated the safety and efficacy of placing serial Plicator implants within 1 cm of the anterior GE-junction for the treatment of GERD in the multi-center setting.

**Methods:** 41 subjects with chronic heartburn requiring daily PPI-therapy were treated at four sites. Subjects received multiple full-thickness plications serially placed in the gastric cardia <1 cm below the GE-junction. At baseline and 6-months post-plication, subjects completed the GERD-HRQL-assessment, GERD medication-use diary, GERD related symptom VAS, 24-hour esophageal pH monitoring, control gastroscopy and manometry.

**Results:** 41 subjects underwent endoscopic full-thickness plication with serial implants (2–3). 40 subjects completed the 6-month follow-up assessment. All procedure-related adverse events occurred acutely (abdominal pain 42%; radiating shoulder pain 20%; chest pain 17%; sore throat 15%). No new adverse events were observed during the follow-up. At 6 months post-procedure, 65% (26/40) of baseline PPI dependent patients remained off daily PPI therapy. Median GERD-HRQL scores were improved at 6-months versus baseline off-med scores (6 vs. 25,  $P < 0.001$ ) and versus baseline on-med scores (6 vs. 11,  $P = 0.02$ ). Median VAS scores were improved at 6-months versus baseline off-med (16 vs. 84,  $P < 0.001$ ) Median esophageal acid exposure improved (9 vs. 11,  $P = 0.02$ ) with normalization of pH noted in 31% of subjects. Median LES resting pressure also improved at 6-months (10 vs. 6,  $P = 0.017$ ). Mean esophagitis grade improved by 48% ( $P = 0.005$ ) at 6-months compared to the mean baseline esophagitis grade.

**Conclusion:** The results of the multi-centre study are similar to six month pilot study results in demonstrating the safety and efficacy of the serial implant technique in reducing esophagitis, PPI use, GERD symptoms, GERD medication use, and esophageal acid exposure.

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### Endoscopic Full-Thickness Plication with Two Serially Placed Implants Improves Esophagitis, GERD Symptoms and Reduces PPI Use and Esophageal Acid Exposure

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**Purpose:** Recently, several endoluminal procedures for the treatment of GERD have been introduced. However, most of these techniques have been abandoned due to either lack of long-term efficacy or serious side effects. In a recently published prospective randomized, sham-controlled trial, the Plicator™ (NDO Surgical, Inc.) proved effective at controlling reflux symptoms and reducing medication use and esophageal acid exposure.

**Methods:** In all studies to date, a single Plicator implant was placed to form a full thickness plication of the anterior gastric cardia. However, in several cases the narrowing of the GE-junction remained incomplete with this technique. Therefore, we evaluated the safety and effectiveness of placing two Plicator implants within 1 cm of the anterior GE-junction for the treatment of GERD.

**Results:** 37 patients underwent endoscopic full-thickness plication using two serially placed Plicator implants. At 6 months post-treatment, the proportion of patients achieving >50% improvement in GERD-HRQL score was 68%. Complete PPI cessation was achieved in 59% of patients. In pH studies conducted at 6-months (N = 29), median percent time pH < 4 decreased 36%, with 28% of patients experiencing pH normalization. Erosive Reflux Disease (ERD) was diagnosed in 21 patients before endoscopic full-thickness plication. 16 patients had NERD before endoscopic full-thickness plication. Six months after endoscopic full-thickness plication the number of subjects with ERD was 15 and the number of subjects without esophagitis was 22. There were no serious adverse events observed. Minor adverse events included abdominal pain (73%), sore throat (54%),

and chest pain (57%). All adverse events resolved spontaneously without intervention.

**Conclusion:** In this study, endoscopic full-thickness plication using two serially placed Plicator implants was both safe and effective in reducing esophagitis, GERD symptoms, GERD medication use, and esophageal acid exposure. When compared to previous studies using a Plicator single implant technique, the Plicator multiple-implant technique demonstrates a similar safety profile and superior efficacy.

## 27

#### Are There Differences in Sensitivity Thresholds to Balloon Distention in the Upper and Lower Esophagus?

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**Purpose:** The proximal and distal esophagus are different with respect to muscle type, structure, innervation, and gradient of calcium channels and nitric oxide concentration. Our aims were: 1) To verify that an improved method of measuring the placement of the balloon catheter does not alter balloon sensitivity parameters, 2) To assess symptoms provoked by barostat balloon distention of the upper and lower esophagus and 3) To compare sensitivity thresholds to balloon distention in the upper vs lower esophagus in normal subjects.

**Methods:** Subjects were randomized to 2 esophageal barostat sessions, performed within a 7-d period. After manometry (using traditional or new measuring technique), subjects underwent Barostat balloon distentions at 5 ml increments at 5 cm above the LES, and 3 cm below the UES. 1st sensation, 1st discomfort, and max pain (request to terminate) were determined, with symptoms also collected. Means were generated and a paired 2-tailed T-test was performed ( $P = 0.05$ ).

**Results:** Data were analyzed from 21 subjects (13 f, 8 m; mean age 27.6 yrs). There were no differences in balloon sensitivity thresholds between sessions (traditional vs new measuring technique) ( $P > 0.05$ ). 1st sensation and 1st discomfort were significantly lower in the proximal vs distal esophagus ( $P < 0.05$ ). Max pain was not different between esophageal regions (traditional method: 33.6 ml distal vs 25.7 proximal,  $P = 0.18$ ; new method: 33.6 ml distal vs 28.6 ml proximal;  $P = 0.44$ ). Distal esophageal balloon distention produced chest discomfort in 20/21 subjects, chest tightness in 11/21, and fullness in 9/21 subjects. In the upper esophagus, chest discomfort was most common (18/21), with chest tightness (14/21) and chest pain (11/21) also produced. Cough was produced in 5/21 subjects in the upper and lower esophagus; burning was produced in 8/21 subjects in the lower and 9/21 subjects in the upper esophagus.

**Conclusion:** Sensitivity thresholds are repeatable and were lower in the proximal vs distal esophagus. Balloon distention produced numerous symptoms, although unfamiliar, in this normal group, the most prominent of which was chest discomfort. Cough and burning were also produced by esophageal balloon distention in the upper and lower esophagus in this normal group, suggesting neurologic reflex pathways are independent of pathologic reflex.

## 28

#### High Cortisol Levels Are Correlated to Low Esophageal Pain Threshold to Balloon Distention in Patients with NERD and Functional Heartburn

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**Purpose:** The relationship between serum cortisol and visceral pain varies dramatically in published studies. In patients with functional GI disorders

(FGID), symptoms are often absent during the night when cortisol is low. However, patients with FGID and low awakening cortisol reported the greatest pain (Ehlert 2005). Rectal balloon distention in patients with IBS vs chronic constipation (CC) vs controls (C) indicated IBS patients had the lowest sensory thresholds than CC and C (Walter et al., 2006). Our aims were: 1) To describe the relationship between serum Cortisol and maximum tolerable pain to balloon distention of the esophagus in patients with functional heartburn (FxHB), 2) To compare cortisol, ACTH, and balloon sensitivity parameters in functional heartburn vs NERD.

**Methods:** 26 patients underwent esophageal balloon distention with MTD (volume and corresponding mean and maximum pressure). 14 patients fit criteria for FxHB and were assessed on 4 occasions ( $N = 56$ ). 12 patients fit criteria for NERD and were assessed once ( $N = 12$ ). Blood samples for serum cortisol and ACTH were collected within 90 min prior to balloon distention. Regression analysis was performed between maximum tolerable pain (ml of balloon volume and corresponding mean and maximum mmHg pressure at MTD) and serum Cortisol levels (ug/dl), and between Cortisol and ACTH levels (pg/ml). Parameters were compared via t-test ( $P = 0.05$  level of significance).

**Results:** There were no differences between FxHB and NERD in mean Cortisol (11.6 vs 9.8 mg/dl), mean ACTH (17.5 vs 16.4 pg/ml), or mean sensitivity parameters (22.7 vs 19.2 ml balloon volume; 29.3 vs 28 mmHg mean pressure; 48.9 vs 41.5 mmHg max pressure; all  $P > 0.05$ ). Therefore all patients were grouped together ( $N = 68$  observations). MTD volume approached significance related to cortisol levels ( $P = 0.07$ ); however, mean pressure at MTD was significantly and inversely related to serum cortisol level ( $r = 0.50$ ;  $P = 0.000122$ ). Maximum balloon pressure at MTD was also significantly and inversely related to cortisol level ( $r = 0.31$ ;  $P = 0.01$ ). As expected, Cortisol and ACTH were significantly related ( $r = 0.60$ .  $P = 1.8 \times 10^{-6}$ ).

**Conclusion:** Overall, higher cortisol levels were significantly related to lower pain threshold to esophageal balloon distention. The significant positive relationship between ACTH and Cortisol indicate that patients had an intact HPA axis. These data imply that adrenal function may play a role in functional GI disease.

## 29

#### The Prevalence of Barrett's Esophagus in Patient with or without GERD Symptoms

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**Purpose:** The incidence of adenocarcinoma of the esophagus is rising rapidly in US, presumable because of the prevalence of intestinal metaplasia of the esophagus (Barrett's esophagus). Millions of Americans have chronic GERD symptoms, and it is still controversial whether to screen these patients with endoscopy in order to identify Barrett's esophagus.

**Methods:** We searched the PENTAX EndoPRO database for the Endoscopy Unit at the University of Texas Medical Branch. We divided the patients into 2 groups: 1) Patients screened because of chronic GERD symptoms. 2) Patients undergoing upper endoscopy for other reasons. Patients with known Barrett's esophagus were also noted. Patients were determined to have Barrett's esophagus if salmon colored mucosa typical of specialized columnar epithelium was described above the gastroesophageal junction. The length of the Barrett's esophagus in this study was reported from 2 cm to 12 cm.

**Results:** There were a total of 5019 EGD's in 4500 patients in our data base from August 2005 to May 2007. 410 patients underwent upperendoscopy because of GERD symptoms that were not responding to PPI therapy. 153 patients were male and 257 patients were female. 27 patients were found have Barrett's esophagus (6.5%). Among the 27 patients with Barrett's esophagus, 17 patients were male and 10 patients were female. No significant age difference in this group was found between patients with and without Barrett's esophagus ( $51.9 \pm 11$  vs.  $53.9 \pm 13$ ).



The total number of patients with EGD performed for other reasons was 4090. 43 patients underwent surveillance for known Barrett's esophagus. 80 patients (1.98%) were found incidentally to have Barrett's esophagus while undergoing endoscopy for another reason, among the patients in whom Barrett's esophagus was found incidentally. The asymptomatic patients with Barrett's esophagus (age  $58 \pm 13$ ) are significantly older than the patients with Barrett's esophagus and GERD symptoms (age  $51.9 \pm 11$ ),  $P < 0.01$ .

**Conclusion:** 1. More cases of Barrett's esophagus were found incidentally, than were found in patients being specifically screened for chronic GERD symptoms. It is low yield to screen patients with chronic GERD symptoms. The asymptomatic patients with Barrett's may account for the high incidence of adenocarcinoma.

2. Although female patients have a high prevalence of GERD symptoms and perhaps seek more medical attention, there is higher yield of Barrett's esophagus in male patients with chronic GERD symptoms.

## 30

### Low Grade Esophageal Eosinophilia in Adults: An Unrecognized Part of the Spectrum of Eosinophilic Esophagitis?

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**Purpose:** Eosinophilic Esophagitis (EE) has traditionally been defined by the presence of greater than 20 eosinophils (eos) per high powered field (HPF) on esophageal biopsy. The clinical significance of 20 eos/HPF or fewer is unknown. We hypothesized that EE is a spectrum and lower eosinophil counts reflect similar disease.

**Methods:** 121 adult patients without a previous diagnosis of EE with esophageal biopsies containing 1 to 20 eos/HPF were identified by retrospective review of a database of patients with esophageal eosinophils on biopsy at a tertiary care center between 2002 and 2006. Phone interviews were conducted to ascertain long term symptom control.

**Results:** Patients with 1–5, 6–12, and 13–20 eos/HPF on esophageal biopsy had similar clinical presentations and endoscopic findings (table). There was no statistical difference among sex, race, and age in patients with 13 to 20 eos/HPF compared to those with 1 to 12 eos/HPF. Over 1/3 of patients that had repeat endoscopy were diagnosed with EE ( $>20$  eos/HPF). Phone interviews conducted with 16 patients (5 with 1–12 eos/HPF) who received swallowed topical corticosteroids found symptomatic improvement in all 16 patients following six weeks of treatment.

**Conclusion:** Patients with a clinical presentation consistent with EE and indeterminate esophageal eosinophils on biopsy should be treated for EE. The number of eosinophils per HPF on biopsy appears to be less relevant than the clinical presentation. Moreover, the current diagnostic value of greater than 20 eos/HPF should be reevaluated.

## 31

### Prevalence of Gastroesophageal Reflux Disease in Patients with Non-Cardiac Chest Pain Presenting to the Emergency Department

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**Purpose:** This study prospectively evaluated the prevalence of Gastroesophageal reflux disease (GERD) in Non-Cardiac Chest Pain (NCCP) patients in the ED

**Methods:** Patients were deemed to have NCCP after evaluation by an emergency physician. Exclusion criteria were: recent history of ischemic events ( $< 6$  months); proton pump inhibitors use, pregnancy; active psychiatric or unstable medical conditions. Study patients underwent upper endoscopy with placement of the wireless Bravo pH capsule (Medtronic Inc., Shoreview, MN) within two weeks of the initial ED visit. Esophageal, gastric or duodenal lesions were noted. The intraesophageal pH readings were recorded for 48 hours. An abnormal pH study was defined as the total% time pH  $< 4$  of over 4 percent on at least one of the two days of study. The prevalence of esophageal acid exposure abnormalities and their corresponding 95% confidence intervals were calculated.

**Results:** We screened 138 consecutive patients with NCCP in four months, 56 patients met exclusion criteria, 82 were eligible and 31 patients consented and participated. There were 19 (61%) females and 12 (39%) males, 9 (29%) Caucasians, 10 (32%) Hispanics, 10 (32%) African Americans and 2 (6%) Asians. The average age was 47 (range 31 to 63) years. Endoscopic findings in the 16 patients were: 3 (19%) had erosive esophagitis, and 3 (19%) had non-erosive esophagitis. Three pH studies were excluded due to premature capsule release, and 28 studies were analyzed. Abnormal esophageal acid exposure were seen in 16 patients (57.1%, CI: 37.0%~77.3%) on one of the two days of monitoring. On day one, 7 out of 12 males (58%) and 6 out of 19 (32%) females had abnormal esophageal acid exposures; on day two, 6 males (50%) and 7 females (37%) were had abnormal studies. Women had both supine and upright reflux: 6 out of 6 (100%) on day one and 5 out of 7 (71%) on day two had both supine and upright reflux. In contrast, men had less supine reflux: 3 out of 7 (43%) day one and 4 out of 6 (67%) on day two had supine reflux, 6 out of 6 (100%) on day one and 6 out of 7 (86%) on day two had upright reflux.

**Conclusion:** We found a 57% prevalence of GERD in NCCP patients presenting to the ED with more women than men with NCCP seen in the ED. Potential gender differences in esophageal acid exposures warrant further investigation.

## 32

### Barrett's Esophagus under Antisecretory Therapy: The Higher the Severity of Dysplasia, the Higher the Likelihood of Regression

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Clinical Features of Patients with 1–20 EOS per HPF

# EOS per HPF	Dysphagia	Food Impaction	Reflux or Heart-Burn	Allergy History£	Peripheral Eosinophilia¥	Findings Suggestive of EE on Endoscopy§	>20 EOS per HPF on F/U Endoscopy
1 TO 5	82.4%	17.6%	52.9%	23.5%	36.4%	41.2%	33.3%
EOS/HPF	(14/17)	(3/17)	(9/17)	(4/17)	(4/11)	(7/17)	(2/6)
6 TO 12	70.0%	27.5%	55.0%	17.5%	47.6%	40.0%	28.6%
EOS/HPF	(28/40)	(11/40)	(22/40)	(7/40)	(10/21)	(16/40)	(2/7)
13 TO 20	81.3%	40.6%	48.4%	31.3%	28.6%	40.6%	44.4%
EOS/HPF	(52/64)	(26/64)	(31/64)	(20/64)	(12/42)	(26/64)	(4/9)

£ Asthma or allergic rhinitis. ¥  $\geq 0.3 \times 10^9/L$  peripheral eos. § Ringed esophagus, furrows, non distal stricture, or whitish exudates

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**Purpose:** Barrett's esophagus (BE) is a pre-malignant condition. Surveillance endoscopy is recommended to detect either high grade dysplasia (HGD) or esophageal adenocarcinoma (EAC) at an early, curable stage. At the moment, treatment of BE is mostly limited to antisecretory therapy. The purpose of this study is to evaluate the history of BE under antisecretory therapy and to determine which pathologic grade at index diagnosis is most likely to regress.

**Methods:** All patients with BE diagnosed or surveyed from 1995 to 2005 at a single medical center were included in the study. All patients with EAC within 6 months of first endoscopy or patients with single endoscopic biopsy results were excluded. The first pathologic report on file was taken as the index pathologic grade. Subsequent pathologic grade was classified as metaplasia (M), low grade dysplasia (LGD), or high grade dysplasia (HGD). All patients were on antisecretory therapy (H2 blocker, proton pump inhibitor or both).

**Results:** A total of 165 patients met study criteria. Most patients were males (160/165, 97%) and white (148/165, 90%). More than half (91/165, 55%) were obese at index diagnosis. Median surveillance length was 50 months. Almost a third (54/165, 32.7%) were between the age of 50 and 59. Initial pathologic grades were as follows: M (97/165, 58.8%), LGD (62/165, 37.6%), and HGD (6/165, 3.6%). Overall, 53.3% had no change in pathologic grade, 35.2% regressed to a lower pathologic grade, and 11.5% progressed to a higher grade. None progressed to EAC; 3.6% (6/165) progressed to HGD and 11.5% (19/165) regressed to normal mucosa. After adjusting for age, BMI, and pathologic grades, those aged 65 and above were 1.5 times (OR 1.5, *P*-value 0.38) more likely to progress. Those with LGD and HGD were 39 times (OR 38.93, *P*-value 0.000) and 57 times (OR 57.0, *P*-value 0.001) more likely to regress respectively.

**Conclusion:** The course of BE may be altered by antisecretory therapy. There were more normalization of BE than progression to HGD or EAC with surveillance under antisecretory therapy. Regression appears to be inversely related to pathologic grade i.e. the higher the index pathologic grade, the higher the likelihood of regression while on antisecretory therapy. Prospective studies are needed to validate these findings.

### 33

#### Esophageal pH Monitoring with Bravo™ Capsule in Patients with Suspected Gastroesophageal Reflux Disease

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**Purpose:** Traditional catheter-based 24-hour esophageal pH monitoring is limited by patient discomfort and a tendency for patients to alter their diet. A catheter-free pH monitoring system (Bravo™) has been developed as a more tolerable method which may also be more sensitive because of its ability to record data over a 48-hour period. Our aim was to evaluate the safety, performance, tolerability of the Bravo™ monitoring system, and the significance of extending pH monitoring to 48 hours.

**Methods:** The records of 112 patients with presumed or definite gastroesophageal reflux disease (GERD) undergoing Bravo™ pH monitoring were reviewed. Bravo™ capsule was placed 6 cm above the endoscopically identified squamo-columnar junction. All patients were instructed to carry the receiver for a 48-hour study period. pH data, patient diaries and charts were reviewed and analyzed.

**Results:** Of 112 patients (73 female), five had the test twice and two had it three times. Of 121 available studies, 107 (88%) were included in the analysis after excluding one case in whom the capsule could not be passed through esophagus, one case with failure of capsule attachment to the esophagus, one case in whom data could not be retrieved from the receiver, four cases with less than 43 hours of recording, four cases with evidence of dislodgement,

and three cases with transmission artifacts. Chest pain was the most common complaint during the study period, reported in 57% of studies. Only one patient reported severe chest pain that necessitated a CT of the chest which was normal. Of 107 studies, DeMeester score was above 14.72 in 56 (52%) and mean AET (the percentage of time the distal esophageal pH is less than 4) was above 4.5% and 5.3% in 54 (50%) and 47 (44%), respectively. Of 94 studies in which AET was available for each day separately, AET was  $\geq 4.5\%$  in 41 and 39 studies on day 1 and day 2, respectively. Twenty-nine studies were positive on both days; 12 were positive only on day 1 and 10 were positive only on day 2. Thus, a 48-hour study increased the sensitivity by 11% compared to 24-hour study.

**Conclusion:** Forty-eight-hour esophageal pH monitoring with Bravo™ capsule is a safe, effective, and tolerable method that may also have a better sensitivity in GERD detection than the conventional 24-hour monitoring system.

### 34

#### Characteristics of Patients with Reflux Esophagitis, Non-Erosive Reflux Disease and Functional Heartburn

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**Purpose:** Patients with non-erosive reflux disease (NERD) account for up to 70% of the gastroesophageal reflux disease (GERD) population and represent a heterogeneous group. Our aim was to compare the demographics and clinical characteristics of patients with reflux esophagitis (RE), NERD, and functional heartburn (FH).

**Methods:** We reviewed the medical records of 81 consecutive patients with frequent heartburn and regurgitation on whom Bravo™ capsule 48-h esophageal pH monitoring was performed after capsule placement under endoscopic guidance. Patients were instructed to stop taking acid-suppressive therapy at least 7 days before the pH study. An abnormal study was defined as either a DeMeester score  $\geq 14.72$  or a mean acid exposure time (the percentage of time pH less than 4)  $\geq 4.5\%$ . Patients with esophageal mucosal injury observed during capsule placement or during a prior endoscopy comprised the RE group. The remaining patients were divided into two groups according to pH monitoring study results: NERD (those with an abnormal pH study) and functional heartburn (FH) (those with a normal pH study). Chi-square and t-test were used to compare categorical and continuous data between groups.

**Results:** Of 81 patients, 28 (35%) were in the RE group, 27 (51%) comprised the NERD group and 26 (49%) met our criteria for the FH group. No statistically significant difference was found between the three groups in distribution with respect to age, prevalence of hiatal hernia, and presenting symptoms, except that patients with RE had more respiratory symptoms (cough, hoarseness, shortness of breath) compared to patients with NERD or FH (See Table), and patients with FH were more likely to be female. Interestingly, only 16 of 28 RE patients had an abnormal pH study.

**Conclusion:** Patients with RE experience more respiratory symptoms compared to patients with NERD or FH. As only 57% of RE patients had an abnormal pH study, factors other than acid exposure may contribute to the development of esophagitis. FH is more common in women than men.

n (%)	RE (N = 28)	NERD (N = 27)	FH (N = 26)
Mean age	48 $\pm$ 14	48 $\pm$ 14	45 $\pm$ 12
Female	15 (54)	16 (59)	23 (89)*
Respiratory symptoms	8 (29)*	2 (7)	2 (8)
Chest pain	14 (50)	17 (63)	17 (65)
Dysphagia or weight loss	8 (29)	4 (15)	4 (15)
Hiatal hernia	10 (36)	12 (44)	9 (35)

\**P* < 0.05

### Utility of Catheter-Free Ambulatory pH Testing on PPI Therapy

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**Purpose:** To determine the utility of performing ambulatory pH testing on proton pump inhibitor (PPI) therapy using a catheter-free system (BRAVO).

**Methods:** All patients referred to our laboratory over a 24-month period for an ambulatory 48-hour pH test and who were on a PPI at least once daily were included. Patients were referred by a combination of gastroenterologists, other subspecialists or primary care providers. The pH capsule was placed during endoscopy, six centimeters above the squamo-columnar junction. Patients were excluded if incomplete data were available or if the patient inadvertently discontinued their PPI before or during the study. Percent acid exposure for each day and for the total study was the primary endpoint. We evaluated both the standard normal cutoff value for percent time pH < 4.0 (5.5%) and a commonly accepted normal value for BID PPI (1.6%). The percentages of patients with abnormal acid exposure on day 1, day 2 and for the total 2-day study period were calculated.

**Results:** 122 of 259 consecutive pH studies (47%) were performed on PPI therapy. 12 patients were excluded from analysis (2 due to probe dislodgement early in the study, 5 due to discontinuation of PPI during the study and 5 because time recorded on one of the two days was less than 12 hours). Of the 110 remaining studies, 71 (65%) were on BID PPI and 39 (35%) on QD. The percentages of patients with excessive acid reflux are presented in the tables.

**Conclusion:** Catheter-free esophageal pH testing in patients on PPI therapy provides complete data in the majority of patients. In this group of patients, 15.5% of studies on BID PPI show ongoing acid reflux (over 48 hours) using the common cutoff of 5.5% and 35.2% using the alternative cutoff of 1.6%. If abnormal reflux on either day is considered pathologic those percentages increase to 23.9 and 43.7% respectively. There was a paradoxical finding of fewer patients with a positive study on QD PPI possibly related to referral bias. Testing using this method provides useful information on the presence of ongoing acid reflux in patients on PPI therapy.

5.5% pH Cutoff (% abnormal)

	Day 1	Day 2	Either Day	Total Study
BID PPI	14.1%	12.7%	23.9%	15.5%
QD PPI	7.7%	7.7%	10.0%	7.7%

1.6% pH Cutoff (% abnormal)

	Day 1	Day 2	Either Day	Total Study
BID PPI	36.6%	29.6%	43.7%	35.2%
QD PPI	23.1%	15.4%	25.0%	20.5%

### Are Patients with Barrett's Esophagus Likely To Develop Cancer or High Grade Dysplasia If They Miss Their Surveillance Endoscopy?

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**Purpose:** Surveillance endoscopy is recommended for patients with Barrett's esophagus (BE). The frequency of surveillance is based on the severity of dysplasia. Nobody knows what happens to patients if they missed their surveillance endoscopy. The purpose of this study is to evaluate the effect of missed surveillance endoscopy on the pathologic grade of BE and to determine those likely to miss surveillance endoscopy.

**Methods:** Patients diagnosed or surveyed for BE between 1995 and 2005 at a single center were evaluated. Patients were included in the study if they had more than 2 endoscopic biopsies, and have missed their surveillance endoscopies by 6 continuous months or more. Patients diagnosed with esophageal adenocarcinoma (EAC) within 6 months of first endoscopy were excluded. All patients were on antisecretory therapy (H2 blocker, proton pump inhibitor or both).

A sub-analysis of those who missed their surveillance endoscopy by twice the current recommended intervals i.e. 6 years for metaplasia (M), 2 yrs for low grade dysplasia (LGD), and 6 months for high grade dysplasia (HGD) was also done.

**Results:** Forty-four patients missed their surveillance endoscopy by at least 6 months. The distribution of the pathologic grades was as follows: M (11/44, 25%), LGD (32/44, 72.7%), and HGD (1/44, 2.3%). Of these, 50% regressed to a lower pathologic grade, 40.9% had no change, and 9.1% progressed to a higher pathologic grade. Four patients regressed to normal mucosa, 1 progressed to HGD and none progressed to EAC.

More than half of these patients (23/44, 52.3%) missed their surveillance endoscopies by twice the current recommended intervals. The initial pathologic grades were as follows: M (3/23, 13%), LGD (19/23, 82.6%), and HGD (1/23, 4.3%). Of these, 60.9% regressed, 34.8% did not change, and 4.3% progressed. None progressed to EAC or HGD but 3 regressed to normal mucosa. After adjusting for age and body mass index (BMI), patients with LGD are nearly seven times more likely to miss their endoscopy (OR 6.56, *P*-value 0.03).

**Conclusion:** Patients with BE on antisecretory therapy may have longer surveillance intervals without an increased risk for progression when compared to current guidelines. Patients with LGD are most likely to miss their surveillance endoscopies. This may be due to the nomenclature used in categorizing LGD. More studies are needed to validate these findings.

### Comparison of Serum Pepsinogens between Patients with and without Reflux Esophagitis

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**Purpose:** Reflux esophagitis (RE) has been considered as one of complications of peptic ulcers before *H. pylori* was discovered. Recently, peptic ulcers are reported to have a close association with *H. pylori* in spite of the fact that the prevalence of *H. pylori* infection is low in RE patients. Serum pepsinogen (PG) is a known marker of gastric mucosal status, including mucosal atrophy. The aim of this study is to evaluate the diagnostic potential of serum PGs in predicting the presence of RE in patients with and without *H. pylori* infection.

**Methods:** A total of 121 patients with RE in whom *H. pylori* infection was diagnosed by 13C-urea breath test (UBT) were recruited. The mean age was 58 years (33–85 years) and 64 were women. All patients underwent a change of the delta 13C value over baseline of more than 2.5 per mil was considered positive. Serum PG concentrations were assayed using PG1 and PG2 Riabead Kits. Age-, gender-, and *H. pylori* status- matched controls without RE were selected.

**Results:** Among 121 patients with RE, 78 had *H. pylori* infection. In *H. pylori*-negative patients, a serum PG1 level was significantly higher in those with RE than without RE ( $54 \pm 20$  vs  $40 \pm 12$  ng/mL, *P* < 0.01). There was no significant difference in a serum PG1 level between *H. pylori*-positive patients with and without RE ( $67 \pm 48$  vs  $60 \pm 29$  ng/mL). Significant differences in a serum PG2 level were not found between patients with and

without RE regardless of H. pylori status. Among H. pylori-positive patients, a PG1/PG2 ratio was significantly higher in RE patients ( $3.5 \pm 1.5$  vs  $2.8 \pm 1.3$ ,  $P < 0.01$ ). The same tendency was also found in H. pylori-negative patients, but the difference did not reach statistical significance ( $5.9 \pm 1.6$  vs  $5.2 \pm 1.4$ ,  $P = 0.06$ ).

**Conclusion:** High serum PG1 levels and PG1/PG2 ratios were more commonly detected in GERD patients in spite of H. pylori status.

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### GERD Treatment with Lansoprazole May Improve Sleep Disorders

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**Purpose:** A link between gastroesophageal reflux diseases (GERD) and sleep disorders in some patients with nocturnal heartburn episodes has been suggested; however, the prevalence of sleep disorders in GERD patients remains unclear. It is also unknown whether PPI therapy for GERD improves sleep disorders. The aim of this study is to investigate the effects of long-term lansoprazole therapy on the symptoms of sleep disorders.

**Methods:** A total of 154 patients who had reflux esophagitis and received PPI therapy (Lansoprazole 15 mg once daily) for more than 24 months were recruited. The mean age was 69 years (39–77 years) and 117 were women. The presence of sleep disorders was defined if the patient required sleeping drugs in at least 4 days a week for more than 3 months. Blood samples were taken in all patients for detecting serum IgG antibody to Helicobacter pylori (HM-CAP).

**Results:** Of 154 patients, 28 had sleep disorders. Zopiclone was prescribed in 5 patients, Quazepam in 3, Triazolam in 8, Zolpidem tartrate in 6, Brotizolam in 5, and Estazolam in one. Medications for sleep disorders were stopped in 6 (22%) patients after lansoprazole therapy. The mean duration to stopping the medication was 5.8 months after the beginning of PPI therapy. Of 28 patients receiving sleeping drugs, 18 were H. pylori positive and 2 of them succeeded in leaving off the medication for sleep disorders. Of 10 H. pylori-negative patients, the medication for sleep disorders became useless in four. All patients treated with Triazolam or Estazolam required continuous medication after lansoprazole therapy. Relief from the medication was accomplished in one of 5 patients treated with Zopiclone, in one of three with Quazepam, in two of six with Zolpidem tartrate, and in two of five with Brotizolam.

**Conclusion:** Relief from the medication for sleep disorders was succeeded in 22% of GERD patients after lansoprazole therapy. Improvement in symptoms of sleep disorders likely resulted from a reduction in GER.

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### Trends of Heller Myotomy Hospitalizations for Achalasia in the United States, 1993–2004

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**Purpose:** Achalasia is a rare chronic disorder of esophageal motor function. Since its introduction in 1993, there has been increasing use of laparoscopic surgical (Heller) myotomy for achalasia, which typically involves a shorter hospital stay. We examined the trends of Heller myotomy hospitalizations in the United States during 1993–2004.

**Methods:** The publicly available Healthcare Cost and Utilization Project Nationwide Inpatient Sample is a representative sample of 5 to 8 million hospitalizations per year in the United States and provides national esti-

mates of hospitalizations by diagnosis or procedure. It was used to study the time trend of Heller myotomy hospitalizations, i.e., those with ICD-9-CM procedure code 42.7 (esophagomyotomy) as the primary procedure and the time trend of achalasia hospitalizations, i.e., those with ICD-9-CM diagnosis code 530.0 as the primary diagnosis. The ICD-9-CM procedure code 42.7 does not distinguish between open and laparoscopic Heller myotomy.

**Results:** The national estimate of Heller myotomy hospitalizations increased from 728 in 1993 to 2,329 in 2004 (+220%). This compared to smaller percent increases in achalasia hospitalizations (2,642 in 1993 and 4,157 in 2004; +57%) and in all hospitalizations in the United States (34,314,213 in 1993 and 38,661,786 in 2004; +13%). Notably, the increase in Heller myotomy hospitalizations ( $N = 1,601$ ) roughly equals to the increase in achalasia hospitalizations ( $N = 1,515$ ). The median length of stay for Heller myotomy hospitalizations decreased from 7 days in 1993 to 2 days in 2004, while the median length of stay for achalasia hospitalizations remained stable (3 days) during this period. In 2004, the mean age of Heller myotomy patients was 50 years and 52 percent were male; 79 percent of Heller myotomy procedures were performed in teaching hospitals and 83 percent were performed in large hospitals.

**Conclusion:** The number of Heller myotomy hospitalizations has been increasing in the United States during 1993–2004. This, along with the decreasing length of stay and the concentration in teaching/large hospitals, likely reflects the widespread use of laparoscopic surgery to treat achalasia.

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### Comparison of Esophageal Motility Parameters as Measured by the New High Resolution Manometry (HRM) vs Traditional Manometry (TM)

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**Purpose:** The 36-channel Sierra esophageal motility catheter simultaneously measures pressure from the UES through the body and the LES. This HRM provides an intuitive advance over the standard 4-channel Konigsberg catheter (TM). Before conclusions can be drawn regarding the efficacy of HRM, comparative manometry data needs to be acquired and analyzed to assure that current standards can be applied to this technical advance. The aims of this study were to compare LES measurement from the nares, LES residual pressure (relaxation), LES pressure, distal amplitude, velocity and duration as measured by HRM and TM in a control population.

**Methods:** Normal subjects were randomized to HRM or TM in a crossover design (7-d period between sessions, 48 h apart). Subjects were intubated via the nares. The station pull-through was performed with Konigsberg probe. The HRM probe was placed into the esophagus and LES without moving the probe. 10 water swallows were performed and measurements were recorded. Physiologic data was compared using paired T-tests ( $P = 0.05$ ).

**Results:** Data were analyzed from 21 normal subjects (13 females, 8 males; mean age 27.6 years). Measurement of the distance of the LES from the nares was significantly different for the HRM vs TM probes (43.3 vs 41.7 cm;  $P = 5.95 \times 10^{-5}$ ). Residual LES pressure, a reflection of LES relaxation with water swallows, was significantly different as measure by the catheters (15.8 vs 1.8 mmHg;  $P = 1.17 \times 10^{-6}$ ; HRM vs TM). Distal contractile pressure with water swallows was also significantly different between HRM vs TM (110.8 vs 94.0 mmHg;  $P = 0.02$ ). LES pressure (36.6 vs 32.1 mmHg;  $P = 0.08$ ), Velocity (4.8 vs 3.8 cm/sec;  $P > 0.05$ ) and Duration (3.7 vs 3.7 sec;  $P > 0.05$ ) were not affected by the type of motility catheter.

**Conclusion:** HRM identifies the LES an average of 1.6 cm closer to the LES than with the TM method. Measurement differences would influence the placement of other probes for testing (ie: esophageal pH sensor, balloon distention), and may correlate to altered motility results. LES relaxation as well as distal contractile amplitude were also affected by catheter type. New normal values, as well as “pathologic” values need to be established using the HRM system in order to diagnose esophageal motility disorders accurately.

# Is There Improvement over Years in the Diagnostic Accuracy of Endoscopic Ultrasound in Evaluating Celiac Axis Lymph Nodes Metastasis in Esophageal Cancers? A Meta-Analysis & Systematic Review

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**Purpose:** To evaluate if technology over years affected the diagnostic accuracy of Endoscopic Ultrasound (EUS) in evaluating celiac axis lymph node (CLN) metastasis in esophageal cancers. This analysis was done by grouping EUS studies into three time periods to standardize the change in EUS technology and also to standardize the change in EUS criteria for lymph node involvement. These time periods were 1989 to 1995, 1996 to 1999, and 2000 to 2006.

**Methods: Study Selection Criteria:** Only EUS studies confirmed by surgery or appropriate prolonged follow-up were selected.

**Data collection & extraction:** Articles were searched in Medline, Pubmed, Ovid journals, CINAHL, Medline nonindexed citations, and Cochrane control trial registry.

**Statistical Method:** Meta-analysis for the accuracy of EUS was found by calculating pooled estimates of sensitivity, specificity, likelihood ratios, and diagnostic odds ratio. Pooling of likelihood ratios and diagnostic odds ratios was conducted by the fixed and random effects models. The heterogeneity of was tested using Cochran's  $Q$  test based upon inverse variance weights.

**Results:** Initial search identified 3980 reference articles, of these, 362 relevant articles were selected and reviewed. Data was extracted from 23 studies ( $N = 1966$ ) which met the inclusion criteria. There were 8 studies for the time period 1989 to 1995. During the time period of 1996 to 1999, there were 10 studies that met the inclusion criteria. Five studies met the inclusion criteria for the time period between 2000 to 2006. All the pooled estimates during the three time periods are given in table 1. The  $P$  for chi-squared heterogeneity for all the pooled accuracy estimates was  $>0.05$ .

**Conclusion:** EUS-FNA is highly specific in diagnosing celiac axis lymph nodes metastasis in esophageal cancers. Over years, the specificity remained very high, while the sensitivity did not improve.[figure1]

Table 1: Pooled diagnostic accuracy estimates of EUS-FNA for different time periods with 95% confidence intervals

Time Period	No. of Studies	Pooled Sensitivity	Pooled Specificity	Pooled LR+	Pooled LR-	Pooled DOR
1989 to 1995	8	57.1% (47.4 - 66.5)	97.5% (95.1 - 98.9)	14.2 (6.1 - 33.0)	0.4 (0.3 - 0.6)	46.0 (14.9 - 142.0)
1996 to 1999	10	77.2% (70.4 - 83.0)	98.3% (97.3 - 99.1)	22.2 (6.3 - 78.5)	0.2 (0.1 - 0.6)	103.5 (27.3 - 392.1)
2000 to 2006	5	59.5% (50.4 - 68.2)	98.1% (96.0 - 99.3)	23.4 (11.7 - 46.6)	0.3 (0.1 - 0.7)	85.7 (36.3 - 202.4)

LR+ = Positive Likelihood Ratio  
LR- = Negative Likelihood Ratio  
DOR = Diagnostic Odds Ratio

# Accuracy of Endoscopic Ultrasound over Time in T-Staging of Esophageal Cancers: A Meta-Analysis and Systematic Review

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**Purpose:** Prognosis and modality of treatment in patients with Esophageal cancers (ECA) depends on the T stage of the tumor. The published data on effect of changes in Endoscopic Ultrasound's (EUS) technology over accuracy of T staging in ECA patients has been varied.

**Aim:** To evaluate the effect of the change in EUS technology over the past two decades on its diagnostic accuracy in T-staging of ECA cancers.

**Methods: Study Selection Criteria:** Only EUS studies confirmed by surgery were selected. EUS criteria used for T staging were: T1- the tumor invades the lamina propria or submucosa, T2- the tumor invades, T3-

the tumor invades the periesophageal tissues, and T4- the tumor invades adjacent structures.

**Data collection & extraction:** Articles were searched in Medline, Pubmed, Ovid journals, and Cochrane control trial registry.

**Statistical Method:** Meta-analysis for the accuracy of EUS was analyzed by calculating pooled estimates of sensitivity, specificity, likelihood ratios, and diagnostic odds ratio. EUS studies were grouped into three time periods to standardize the change in EUS technology and also to standardize the change in EUS criteria for tumor staging. These time periods were 1986 to 1994, 1995 to 1999, and 2000 to 2006. Pooling was conducted by both the fixed and random effects models.

**Results:** Initial search identified 3,730 articles, of these, 389 relevant articles were selected and reviewed. 43 studies ( $N = 2558$ ) which met the inclusion criteria were included in this analysis. Pooled accuracy data for T staging over last two decades is shown in table 1. All the pooled estimates calculated by fixed and random effect models were similar. The  $P$  for chi-squared heterogeneity for all the pooled accuracy estimates was  $>0.10$ .

**Conclusion:** EUS has excellent sensitivity and specificity in accurately diagnosing T stage in a patient with ECA. Over the last two decades, the specificity of EUS in diagnosing T stage remained high ( $\sim 98\%$ ). The sensitivity of EUS for T staging slightly improved for T1 and T4 during the past two decades. EUS should be strongly considered for T staging of ECA.[figure1]

Table 1: Accuracy of EUS with confidence intervals to stage esophageal cancers over the past two decades

Year	No. of Studies	Pooled Sensitivity	Pooled Specificity	Pooled LR+	Pooled LR-	Pooled DOR
1986 to 1994	17	80.4% (75.2 - 84.6)	99.2% (98.4 - 99.7)	41.6 (5.1 - 283.3)	0.26 (0.14 - 0.43)	161.9 (60.7 - 545.7)
1995 to 1999	11	83.9% (76.3 - 90.2)	98.4% (98.4 - 99.8)	36.4 (16.5 - 77.8)	0.21 (0.09 - 0.47)	299.9 (107.8 - 834.1)
2000 to 2006	5	82.4% (72.8 - 89.5)	100.0% (99.1 - 100.0)	89.5 (22.0 - 361.1)	0.27 (0.16 - 0.47)	261.2 (81.4 - 838.5)

LR+ = Positive Likelihood Ratio  
LR- = Negative Likelihood Ratio  
DOR = Diagnostic Odds Ratio

# Comparison of Sensed Acid Reflux Event Characteristics among the Different GERD Groups

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**Purpose:** Proximal migration, nadir of pH and duration of acid reflux have been shown to increase the likelihood of experiencing a sensed reflux event (SRE). Thus far, no studies compare SRE characteristics among different GERD groups.

The aim of our study was to compare characteristics of SRE among the different GERD groups.

**Methods:** Patients with typical heartburn symptoms at least 3 times a week for the last 3 months were recruited. Upper endoscopy and pH testing were used to classify the three groups: Erosive esophagitis (EE), Nonerosive reflux disease (NERD) and Functional heartburn (FH). Patients underwent esophageal pH testing using a multiple-sensor pH probe (6.11, 16 cm > LES). All reflux events with pH < 4 at sensor 6 cm > LES that correlated with symptoms were considered as SRE. Their characteristics were compared among GERD groups.

**Results:** A total of 22 patients had EE, 15 NERD, and 13 FH (M/F - 20/2, 12/3, 5/8, mean age  $-51.5 \pm 3.7$ ,  $50.1 \pm 4.2$ ,  $50.3 \pm 3.8$ , respectively). During the pH test, 97 SREs were detected at pH sensor 6 cm > LES. The proximal extent of SREs was significantly higher in the FH group compared to NERD and EE (16 cm vs  $14.26 \pm 0.67$  cm, 16 cm vs  $12.73 \pm 0.53$  cm, respectively,  $P < 0.03$ ). The pH nadir of SREs was significantly higher in the FH group compared to NERD and EE ( $2.32 \pm 1.16$  vs  $1.31 \pm 0.18$ , and  $2.32 \pm 1.16$  vs  $1.16 \pm 0.12$  respectively,  $P < 0.01$ ). The duration and reduction in pH

and number of preceding reflux events 1 hour before an SRE was similar among the groups. The number of preceding acid reflux events 2, 3, and 4 hours prior to an SRE was significantly lower in the FH group compared to NERD and EE, 2 hours ( $5.57 \pm 4.1$  vs  $15.64 \pm 9.2$ ,  $5.57 \pm 4.1$  vs  $14.42 \pm 9.8$  respectively,  $P < 0.05$ ), 3 hours ( $8.80 \pm 4$  vs  $25.60 \pm 12.5$ ,  $8.80 \pm 4$  vs  $21.19 \pm 12.4$  respectively,  $P < 0.01$ ), and 4 hours ( $11.60 \pm 4.4$  vs  $31.30 \pm 15.9$ ,  $11.60 \pm 4.4$  vs  $26.64 \pm 15.7$ , respectively,  $P < 0.01$ ).

**Conclusion:** Patients with FH demonstrated the highest proximal extent of SREs but a higher pH nadir and fewer reflux episodes prior to an SRE compared to NERD and EE. The study suggests that proximal extent of an acid reflux event is the most important physiological factor for symptom generation

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### Is There a Difference in the Prevalence of *Helicobacter pylori* Infection between Short-Segment and Long-Segment Barrett's Esophagus?

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**Purpose:** Recent studies suggest that the length of Barrett's esophagus (BE) is a risk factor for neoplastic progression. Patients with long-segment Barrett's esophagus (LSBE) are at higher risk for development of dysplasia and adenocarcinoma of the esophagus when compared with short-segment Barrett's esophagus (SSBE), which suggests that different pathophysiological mechanisms may be involved in SSBE and LSBE. To date, the role of *H. pylori* infection in the development of BE is still unclear. We aimed to investigate by meta-analysis if any difference exists in the prevalence of *H. pylori* infection between SSBE and LSBE.

**Methods:** Observational studies comparing the prevalence of *H. pylori* infection or *cagA*+ *H. pylori* strains in patients with SSBE (length  $<3$  cm) and LSBE (length  $\geq 3$  cm) conducted in adult populations and published in all languages were identified through MEDLINE, EMBASE and Cochrane database searches until week 21, 2007. *H. pylori* infection required confirmation by histology and/or serology and/or RUT and/or culture. Primary outcome was the prevalence of *H. pylori* infection in SSBE and LSBE. Secondary outcome was the prevalence of *cagA*+ *H. pylori* strains in SSBE and LSBE. Studies were excluded if lacking raw data for outcome of interest or were duplicate publications. Summary effect size was calculated as odds ratios (OR) and 95% confidence intervals (CI) by the random-effects model using Review Manager 4.2.8.

**Results:** Of 458 citations, 13 studies met inclusion criteria. 825 patients with SSBE and 470 with LSBE were included for analysis. The prevalence of *H. pylori* infection was significantly higher in SSBE than in LSBE [39.6% (327/825) and 29.6% (139/470) respectively, OR = 1.49, 95% CI 1.02–2.18,  $P = 0.04$ ], and homogeneity was seen between studies ( $P = 0.14$ ). The results from 4 studies in *H. pylori* positive patients showed no difference in *cagA*+ *H. pylori* strains between SSBE and LSBE [36.7% (18/49) and 37.8% (14/37) respectively, OR = 0.51, 95% CI 0.08–3.04,  $P = 0.46$ ], with homogeneity ( $P = 0.14$ ).

**Conclusion:** The prevalence of *H. pylori* infection in LSBE is significantly lower than in SSBE, which suggests that *H. pylori* infection plays a different role, if any, in these two subtypes of BE and does not "protect" in patients with SSBE. Current evidence does not confirm a role for *cagA*+ in subtypes of BE although the sample size was small. Large prospective studies are needed to confirm these results in the future.

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### Omeprazole Induces a Transepithelial Leak in Gastric Mucosa

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**Purpose:** Having observed a paracellular leak to oral sucrose in esophagitis patients, we tested if PPI therapy would decrease (paracellular) sucrose leak by allowing for mucosal healing.

**Methods:** 23 study subjects presenting to their primary care physician with symptoms of GERD were placed on an 8 week course of esomeprazole (40 mg daily). Subjects were PPI and H-2 blocker naive. All subjects reported symptom alleviation by 4 weeks. Before beginning esomeprazole therapy and at the end of therapy, subjects consumed at bedtime a solution of the disaccharide, sucrose (100 gms in 200 cc tap water), and collected an overnight urine specimen. Sucrose, as a disaccharide, can enter the bloodstream only by leaking paracellularly out of the upper GI lumen. Once in the blood, sucrose is filtered quantitatively into urine. Sucrose concentration in urine was measured by enzymatic/spectrophotometric means. The sucrose concentration  $\times$  the total urine volume yields the total amount of sucrose in the urine, which equals the amount of sucrose which leaked paracellularly from the upper GI lumen.

**Results:** We observed that 17 of 23 patients exhibited a marked increase in sucrose leak by 8 weeks of omeprazole therapy (667% increase). Similar sucrose leak is observed after only 8 days of esomeprazole therapy. Considering all 23 patients, the Wilcoxon Signed Rank Test indicated a significant increase in sucrose leak ( $P = 0.007$ ). In rat gastric mucosa, 200  $\mu$ M omeprazole induces an immediate paracellular leak to D-mannitol, with a simultaneous decrease in transepithelial electrical resistance. Both phenomena indicate that omeprazole is likely producing a tight junction leak in gastric mucosa.

**Conclusion:** PPI therapy may be associated with a paracellular leak in the acid secreting region of the stomach. Future studies will examine the characteristics of this leak and the mechanism by which omeprazole induces the leak.

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### High Prevalence of Eosinophilic Esophagitis in Inflammatory Bowel Disease

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**Purpose:** Eosinophilic esophagitis has been reported in association with asthma and celiac disease but not with inflammatory bowel disease (IBD). We noted in our practice a frequent association between IBD (Crohn's disease or ulcerative colitis) and eosinophilic gastrointestinal diseases (EG) especially eosinophilic esophagitis (EE).

**Methods:** Retrospective chart review of our outpatient pediatric gastroenterology practice. We looked at the pathology reports of our active patients with IBD and selected the ones with EG. Two pathologists confirmed the histological diagnosis of both IBD and EG. We reviewed the indications for the biopsies, age at diagnosis, gender, type of IBD, sequence of the diagnoses and medication history.

**Results:** We have 3800 active patients, out of these 357 had IBD and 151 had EE. We found 18 IBD patients who also had EG including 14 with EE. Thus the prevalence of EG in our IBD population is 5.0% and EE 3.9%. All EG patients were diagnosed simultaneously or after the diagnosis of the IBD. There was no relationship between EE and age, gender, type of IBD and medication history.

**Conclusion:** EE has been reported to have a prevalence of 1–4 per 10,000 children in the USA and thus the relative risk of EE in our IBD population ranges from 97 to 390 compared with the general population. In pediatric patients with IBD, we found a high prevalence of EE. A larger study should be helpful in confirming this observation and may improve our understanding of the pathophysiology of both diseases.

### Inter-Observer Agreement between Multi-Channel Intraluminal Impedance-pH (MII-pH) Software Analysis and an Experienced MII-pH Test Reviewer

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**Purpose:** Over the past decade, new technologies have emerged to evaluate gastroesophageal reflux disease (GERD). One such technique is the 24-hour MII-pH study. This test was designed to detect both acid and non-acid reflux (NAR). A significant drawback of this technique is that reviewing impedance tracings that were collected over a 24-hour period can be cumbersome and time consuming. In an attempt to make this task easier, one of the manufacturers of this device has created a software tool to identify impedance detected reflux episodes based on a number of published parameters. To the best of our knowledge, the utility of an experienced reviewer hand-editing MII-pH tracings after the software analysis has never been evaluated.

**Methods:** We randomly selected 20 MII-pH studies performed at our institution on patients that were taking a proton-pump inhibitor twice daily. We ran the proprietary software analysis tool (Sleuth™, Sandhill Scientific, Inc., Highlands Ranch, CO) on all of these studies using the same pre-programmed parameters. An experienced reviewer of MII-pH studies (DDF) reviewed all the tracings. The reviewer had the ability to add or delete reflux episodes that had been detected by the software tool. We separately recorded the computer and reviewer's analysis in regards to the total number NAR episodes. We determined whether the study was considered positive or negative based on published criteria of NAR. We used Cohen's kappa coefficient to evaluate the inter-observer agreement between the software analysis and the reviewer's over-read.

**Results:** The MII-pH software reported significant NAR in 10 of 20 patients. The reviewer diagnosed significant NAR in 9 of 20 patients. The kappa coefficient for NAR between the software analysis and the reviewer's over-read was 0.9. The one study for which there was a discrepancy between the software and the reviewer had a difference of 11 impedance detected reflux episodes with the software marking more reflux episodes than the reviewer.

**Conclusion:** We demonstrate excellent inter-observer agreement between the software analysis of impedance detected NAR and a hand-edit of that analysis by an experienced reviewer. This finding may lend support to the notion that using software analysis alone is likely adequate to identify clinically significant NAR when using the 24-hour MII-pH system.

### Rebamipide Improves Salivary Gland Function and Saliva Transit to the Distal Esophagus

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**Purpose:** The major abnormalities associated with the development of GERD are related to incompetence of the antireflux barrier and impairment of esophageal luminal clearance after reflux. Although saliva plays an important role in esophageal acid clearance, facilitation of acid clearance has only been addressed via work on various medications which have been shown to have prokinetic effects on the esophagus. This study therefore aimed to investigate the efficacy of a gastro-protective agent, rebamipide, on the function of salivary glands.

**Methods:** Ten healthy volunteers underwent salivary gland scintigraphy twice with one-week interval. The subject is asked to take a rebamipide tablet at a dose of 100 mg 90 minutes before the beginning of the second scintigraphy. Following intravenous injection of <sup>99m</sup>Tc-pertechnetate, anterior sequential imaging was performed every minute for 40 minutes. At 20 minutes after injection of radionuclide, a lemon candy was administered intraorally to stimulate salivary secretion. Regions of Interests (ROI) were selected on the individual submandibular and parotid glands, oral cavity, and the pharynx and the upper esophagus. Time activity curves were drawn for each of these. Washout ratio was examined as a functional parameter. For the evaluation of saliva transit, time activity curves obtained from the ROI of pharynx and upper esophagus were analyzed.

**Results:** The mean washout ratio was 57.8% in the parotid gland and 43.8% in the submandibular gland. If the washout ratios of less than 50% and 36% are defined as functional disorders of parotid and submandibular glands, respectively. After administration of rebamipide, the increased washout ratio (more than 10 points) was found in 5/10 subjects (50%) in submandibular glands and in 1/10 (10%) in parotid glands. Saliva transit from the oral cavity to the esophagus was also improved after administration of rebamipide in 60% of subjects.

**Conclusion:** We concluded that rebamipide might be one of therapeutic options for low salivary excretion, especially for submandibular glands.

### Proximal Black Esophagus: A Case Report

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**Purpose:** Necrotic esophagus (also known as "black esophagus") is a rare clinical entity with fewer than 100 cases reported in the literature. Endoscopically, the esophageal mucosa is dark or black with a macerated appearance. Pathologic review shows mucosal and submucosal necrosis. The majority of published cases of black esophagus describe the lesion in only the distal esophagus or encompassing the entire length of the esophagus. To the best of our knowledge, there have been no reported cases of black esophagus confined to the proximal esophagus.

Our patient is a 79 yo male who presented initially to another hospital with chest pain associated with lightheadedness, diaphoresis and dyspnea. He was found to be bradycardic and received a dose of atropine. An ECG showed changes consistent with an inferior myocardial infarction. The patient was given aspirin, heparin, a beta-blocker and two doses of reteplase and was transferred to our facility. Four hours after the onset of chest pain the patient had a coronary catheterization at our institution. That study revealed an 80% obstructing circumflex lesion and a 100% proximal right coronary occlusion. PTCA was performed and a drug-eluting stent was deployed into the distal circumflex artery. Clopidogrel was initiated. Several hours later, the patient experienced a single episode of hematemesis. An urgent EGD was performed and showed black macerated esophageal mucosa with adherent clot in the proximal esophagus. The abnormal tissue was circumferential and was 5 cm in length. The patient was started on twice daily PPI therapy and his other medications were continued. He was later discharged without further complication.

The rarity of black esophagus is likely due to the extensive arterial blood supply of the esophagus. It has been hypothesized that low-flow states may lead to transient esophageal ischemia with free radical formation and subsequent tissue injury upon reperfusion. In this patient, the isolation of black esophagus to the proximal esophagus may have been due to thromboembolism or hypotension associated with his acute coronary event.

### 5-ALA Photodynamic Therapy Eliminates Resistant Barrett's Cells

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**Purpose:** Photodynamic therapy (PDT) with sodium porfimer has been shown to decrease both high grade dysplasia and cancer formation in Barrett's esophagus. However, we have previously shown that sodium porfimer mediated PDT is not as effective in patients who are p16 deficient which is important in cell cycle regulation. p16 was associated with a substantial risk of treatment failure defined as persistence of high-grade dysplasia or advancement to cancer. Recently, 5-amino levulinic acid (ALA) has become available for use in the United States. It is important to determine if ALA mediated PDT has advantages over sodium porfimer mediated PDT other than shorter duration of cutaneous phototoxicity and decreased stricture formation. Our aim was to determine if ALA mediated PDT cell killing was independent of p16 status.

**Methods:** A Barrett's epithelial cell line immortalized with H-Tert (human telomerase) was provided to us (RF Souza, Texas Southwestern) which has been described as having normal cell functions other than an absence of p16 expression. We used an adenovirus-mediated p16 to infect and re-introduce p16 expression to this cell line. We then compared the effect of PDT with ALA in cells with and without p16. After the cells were established in culture, ALA was provided in concentrations of 0, 2.5, 5, 10, 25, 50, 100, and 250 µg/ml and incubated for 6 hours prior to photoradiation with a broadband xenon light source for a total of 20 J/square cm. Cells were then observed for 4 days after which cell death was assessed with propidium iodide.

**Results:** 5-ALA mediated cell death was similar in both p16+ and p16- Barrett's epithelial cells ( $P > 0.05$ ). There was no significant difference in cell death at any concentration of ALA. Control cells had less than 5% cell death while those that were treated with 50 µg/ml of 5-ALA had about 20% cell death. Treatment with either 100 or 250 µg/ml of 5-ALA produced 90% cell death. The LD50 for 5-ALA was 68 µg/ml.

**Conclusion:** 5-ALA mediated PDT appears to kill Barrett's cells resistant to sodium porfimer mediated PDT. 5-ALA may be able to eliminate Barrett's epithelium in those 20% of patients with high grade dysplasia who have failed sodium porfimer.

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### Gastroesophageal Reflux during Sleep: Does REM Sleep Provide a Protective Effect?

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**Purpose:** The purpose of this study was to assess the prevalence of reflux events over each third of the sleeping interval and to assess whether reflux events may be affected by sleep stages.

**Methods:** Twenty-four individuals with self-reported sleep disturbance and 40 controls without symptoms of sleep disorders or heartburn were studied for two nights via polysomnographic evaluations that included distal esophageal pH recordings. Two PSG recordings were separated by at least two weeks for each participant. For this study we analyzed a subset of participants who had at least one reflux event ( $N = 15$ ). Out of 15 subjects 6 were unrefreshed sleepers with self-reported sleep disturbance and 9 were controls with no sleep disturbance.

**Results:** A total of 40 reflux events were noted in sleep, out of which 20 events are noted in the first 3rd of the sleeping interval, 16 events noted in the second 3rd of the sleeping interval and 4 events noted in the final 3rd of the sleeping interval. The total number of events in the first 3rd of the sleeping interval were significantly higher than final 3rd of the sleeping interval ( $P < .05$ ). There was no significant difference in the number of reflux events in the first and second parts of the sleeping interval. We also analyzed the data to determine if there was any impact of sleep stage on reflux events. We calculated the percent of sleep stages in each third of the night. The amount of deep sleep in the 1st third of the sleeping interval is significantly more than the second third ( $P = .002$ ) and final third of the sleeping interval.

( $P < .001$ ). The amount of REM sleep in final third of the sleeping interval is significantly greater than in the 1st third of the sleeping interval. ( $P < .001$ ) and 2nd third of sleeping interval ( $P = .035$ ). Reflux events persisted into the 2nd third of the sleeping interval when the percent of both REM and deep sleep is very low and stage 2 is dominant. The arousal index didn't significantly differ between the 1st and 3rd part of the sleeping interval. ( $P = .728$ )

**Conclusion:** 1) GER is more common in the first third of the sleeping interval compared to the third portion of the sleeping interval.

2) Reflux events may be affected by the stage of sleep with REM sleep possibly providing a protective effect against GER.

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### The Impact of Recent Developments in the Management of GERD: A Retrospective Cohort Study

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**Purpose:** Recent developments may alter the approach to patients presenting with gastro-esophageal reflux (GERD)-like symptomatology. A recently proposed revised histological definition of Barrett's esophagus (Vakil et al. 2006) includes all types of esophageal columnar metaplasia, with or without intestinal type metaplasia. Also, adult eosinophilic esophagitis may be more prevalent than previously recognized in patients with GERD-like symptomatology. The aim of this study was to quantify the impact of these contemporary realizations on a general Gastroenterology multi-physician practice.

**Methods:** All patients having a gastroscopy for an indication of GERD-type symptoms over a 1-year period ending November 2006 were considered. Patients were excluded if they had had a previous gastroscopy. Medical charts and endoscopic reports were retrospectively reviewed, while prospective audits of all available endoscopic images (grading of esophagitis and endoscopically suspected esophageal metaplasia (ESEM)) and esophageal biopsies were performed using standardized preset criteria.

**Results:** A total of 353 patients fulfilled the study criteria. Typical symptoms of heartburn and regurgitation were found in 87.7% of patients and 23.2% of patients respectively. In addition, atypical chest pain was found in 4.2% of patients, dysphagia in 9.4% of patients, nocturnal symptoms in 11.3% of patients, sleep disturbance in 2.9% of patients, asthma in 1.3% of patients, cough in 2.6% of patients, and hoarseness in 5.5% of patients. 26% of patients were found to have erosive esophagitis at endoscopy, and 11.6% had ESEM. Histological evaluation was available for 65 patients (18.4%). 13.8% of these patients met traditional criteria for Barrett's, exhibiting intestinal-type metaplasia. In contrast, 73.8% of these patients fulfilled the proposed new consensus definition of Barrett's. Five patients (7.6%) met study criteria for eosinophilic esophagitis ( $> 20$  eosinophils/hpf), 4 of whom had not been recognized on the initial pathology report.

**Conclusion:** GERD is an evolving clinical entity. Amongst patients presenting with typical GERD symptoms, the prevalence of Barrett's esophagus, using a revised definition, may increase markedly (over 5 fold increase in this study). In addition, awareness of an overlap with eosinophilic esophagitis may lead to an increase in the prevalence of this diagnosis. Prospective studies of the management implications of these findings are warranted.

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### Predictors of Erosive Esophagitis in Patients with Symptoms of Gastroesophageal Reflux Disease (GERD)

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**Purpose:** To evaluate variables and build a model for prediction of erosive esophagitis (EE) in adults with frequent heartburn (HB).



**Methods:** A post-hoc analysis was conducted on data from a multicenter, open-label study (D9612L00083) in which patients aged 18–70 y who had a history of HB ( $\geq 2$  d/wk for the past week and on average for the past 3 months) underwent endoscopy and symptom assessment at baseline followed by treatment with esomeprazole 40 mg once daily for 4 weeks. For the post-hoc analysis, the following potential predictors of EE at baseline were considered: age; sex; race; body mass index (BMI); *Helicobacter pylori* status; duration of GERD; history of EE; baseline frequency and severity of HB, acid regurgitation, dysphagia, and epigastric pain; and patient-reported time to HB relief with antacids and  $H_2$ -receptor antagonists. Each variable was tested separately in a univariate logistic regression model ( $\alpha$ -level, 0.05) with the presence of EE as the dependent variable. From the 4 candidate models generated by stepwise logistic regression and backward elimination, a multivariate model was selected using Akaike's information criterion. The final model was internally validated using "leave one out" cross-validation.

**Results:** Of 399 patients who had baseline endoscopy, 205 (51.4%) had EE. Full data for modelling were available for 180 patients with and 178 without EE. In the univariate models, older age, male sex, higher BMI, greater HB frequency and severity, greater acid regurgitation severity, white race, longer history of GERD, previous history of EE, and faster time to HB relief with antacid use were significantly predictive of EE ( $P < 0.05$ ). The multivariate model selected included the variables of age, sex, HB frequency, race, EE history, and time to relief of HB with antacid use. The c-index of the model using cross-validation was moderate at 0.76. At a sensitivity of 80%, the model provides specificity of 53%, a positive predictive value of 63%, and a negative predictive value of 72%. The model included a novel predictor in time to HB relief with antacid use. Patients whose HB symptoms were relieved within 0–15 minutes of antacid use had 5 times the odds of having EE versus those who had no relief with antacid use.

**Conclusion:** Modelling of this type can help predict which types of patients presenting with GERD symptoms have EE and may aid physicians in diagnostic decisions and the selection of appropriate pharmacological therapy.

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#### Predictors of Heartburn (HB) Resolution in Patients with Gastroesophageal Reflux Disease (GERD) Symptoms

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**Purpose:** To evaluate variables and build a model to predict HB resolution in patients with GERD symptoms treated with esomeprazole 40 mg once daily.

**Methods:** A post-hoc analysis was conducted on data from a 4-wk, multicenter, open-label study (D9612L00083) in adults with frequent HB ( $\geq 2$  d/wk for past 7 d and on average for past 3 mo) with or without erosive esophagitis (EE). HB severity was rated from 1 (mild) to 4 (severe) at baseline and post-treatment. HB was considered resolved if the patient indicated 'none' on the final symptom questionnaire. Potential predictors of HB resolution were evaluated: age; sex; race; body mass index; *Helicobacter pylori* status; time with GERD; history of EE; baseline frequency and severity of HB, acid regurgitation, dysphagia, and epigastric pain; and patient-reported time to HB relief with antacids/ $H_2$ RAs. Each variable was tested separately in a univariate logistic regression model ( $\alpha$ -level, 0.05). A multivariate model was selected using Akaike's information criterion from among 4 candidate models generated by stepwise logistic regression and backward elimination. The final model was internally validated by "leave one out" cross-validation.

**Results:** The analysis included data from 179 patients with and 177 patients without EE. In the univariate models, male sex, white race, less severe and no dysphagia, less frequent and less severe epigastric pain, and faster relief of HB with antacid use were predictive of HB resolution ( $P < 0.05$ ); *H. pylori*<sup>+</sup> status was not significant ( $P = 0.053$ ). The multivariate model included the variables: baseline severity of HB and epigastric pain, time to HB relief with antacids, *H. pylori* status, and race. Greater HB severity and lesser severity of epigastric pain at baseline, faster HB relief with antacids, *H. pylori*<sup>+</sup> status,

and white race were associated with HB resolution. The c-index of the model using cross-validation was low at 0.57. At a sensitivity of 80%, the model provides specificity of 36%, a positive predictive value of 64%, and a negative predictive value of 56%. The model included a novel predictor in time to HB relief with antacids. Patients whose HB symptoms were relieved within 15 minutes of antacid use had 2.9 times greater odds of HB resolution with esomeprazole than those who had no relief with antacids.

**Conclusion:** This model identified some variables that may predict a response to treatment, but the low discriminative ability underscores the difficulty in such predictions.

## 55

#### Current Trends in Clinical Utility of Esophageal Motility Studies

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**Purpose:** To evaluate the utility of esophageal motility studies in clinical practice.

**Methods:** Clinical and manometric data from 200 consecutive subjects referred for esophageal motility study from our gastroenterology practice starting January 2001 through December 2005 were reviewed in this study. Each subject underwent manometric evaluation using water perfused manometry. Motility study was considered to be of 1) high clinical utility if specific clinical entity was identified on manometry resulting in appropriate therapeutic intervention, 2) low clinical utility if specific clinical entity was identified on manometry without a change in therapy and 3) limited clinical utility if motility study was normal.

**Results:** The 200 subjects underwent 206 esophageal motility studies during the study period. Mean age was 42 years (range: 18–87) with 130 (65%) being females. Major referral indications included (A) dysphagia (65 of 206, 32%), (B) intractable gastroesophageal reflux (27%), (C) non-cardiac chest pain (NCCP) not relieved by therapeutic trial of PPIs and/or normal pH study (19%), (D) dysphagia associated with NCCP (13%) and (E) pre-operative evaluation for fundoplication (9%). Major manometric findings were ineffective motility disorder; IMD (62 of 206 studies, 30%), diffuse esophageal spasm; DES (23%), achalasia (12%), hyperkinetic motility disorder (7%), DES with ineffective motility (4%), scleroderma esophagus (4%) and nutcracker esophagus (2%).

In 96 (47%) of 206 instances, manometric evaluation was of high clinical utility resulting in appropriate therapeutic intervention. This was significantly more common in subjects with NCCP and/or dysphagia ( $P < 0.05$ ). Manometric findings of DES and achalasia were associated with high clinical utility ( $P < 0.05$ ). Manometric evaluation was of low and limited clinical utility in 40% and 13% instances respectively. Motility study was of low clinical utility in subjects presenting with intractable reflux and findings suggestive of IMD ( $P < 0.05$ ).

**Conclusion:** A) Esophageal motility studies have emerging clinical utility in management of patients with non-cardiac chest pain and absence of reflux allowing a positive diagnosis; B) Manometric studies continue to be of high utility in management of patients with dysphagia as a primary complaint; C) Ineffective motility disorder, a new manometric disorder has a high association with gastroesophageal reflux disease but low clinical utility except when planning antireflux surgery.

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#### Multichannel Intraluminal Impedance (MII) Can Make a Diagnosis of Achalasia; A Comparison of MII in Achalasia Versus Normals

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**Purpose:** Achalasia is the most thoroughly studied of the esophageal motility disorders. Manometric criteria include an aperistalsis esophageal body (always required), elevated lower sphincter pressure, high residual pressure and elevated esophageal pressures relative to gastric. The latter three are not required to make the diagnosis. Using these criteria alone some patients are difficult to classify. Multichannel Intraluminal impedance (MII) is combined with traditional manometry (MII-EM) to characterize diseases in terms of pressure and/or transit abnormalities and anecdotally appears to have a characteristic pattern in achalasia. The aims of our study were to describe the MII characteristics of achalasia and compare to patients with normal esophageal manometry.

**Methods:** A retrospective review of all patients with MII-EM testing done at our esophageal lab from 7/03–12/06 identified patients with achalasia and those with a normal manometry. Baseline and post swallow impedance for 10 liquid and 10 viscous swallows in both groups were measured. Descriptive statistics were used for describing frequencies and T test for the differences between the means. Exclusion criteria included incomplete records and previous treatment for those in the achalasia group.

**Results:** 74 eligible patients with achalasia and 172 normal were identified. Achalasia patients had no normal bolus transit. The baseline impedance (expressed in Ohms ( $\Omega$ ) as means  $\pm$  SE) in the achalasia and normal group was  $1114 \pm 99$  v/s  $2130 \pm 73$  respectively ( $P < 0.01$ ). This changed to  $483 \pm 40$  v/s  $1853 \pm 63$  after 10 liquid swallows and  $450 \pm 99$  v/s  $2012 \pm 55$  after 10 viscous swallows respectively (pre post swallow,  $P < 0.01$  for achalasia,  $P = ns$  for normals).

**Conclusion:** Patients with achalasia have no normal bolus movement with MII, low baseline impedance that progressively decreases after multiple swallows in contrast to normal who have stable impedance even after multiple swallows. This MII triad is diagnostic of achalasia. These MII findings are likely due to a dilated fluid filled esophagus at baseline and the inability to effectively clear a bolus in achalasia. MII allows confirmation of manometric diagnosis in difficult cases. Further study is required to determine if MII can make the diagnosis of achalasia independent of manometry.

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### The Evaluation of Definitive Radiation Therapy for Patients with Stage II-III Squamous Cell Carcinoma of the Esophagus

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**Purpose:** The aim of this study is to evaluate the outcome of the patients with stage II-III esophageal cancer treated with radiation therapy.

**Methods:** Between 1999 and 2006, 87 patients with squamous cell esophageal carcinoma were treated with radiation therapy (RT) or concurrent chemoradiotherapy (CRT) at Gunma University Hospital. Seventy-four patients were men and 14 patients were women, and the median age was 71 years (range: 48–93 years). According to TNM staging system (UICC, 2002), 29 patients were stage II (IIA: 23, IIB: 6), and 58 patients were stage III. Radiation therapy consisted of 40–46 Gy with anteroposterior opposing field including the primary tumor and positive regional lymphnodes with optimal margins with conventional fraction followed by external beam boost up to 50–70 Gy (median: 64 Gy). Chemotherapy was administered concurrently with radiation therapy to 50 patients, and the 30 patients received the regimen contained cisplatin or nedaplatin (CRT-PT) and the 20 patients received the regimen consisting of docetaxel (CRT-DOC).

**Results:** At the end of this study, there were 27 survivors with a median follow-up period of 20 months (range: 6–85 months). The 2- and 3-year disease specific survival rates (DSS) were 44% and 29% for all 87 patients, 71% and 44% for stage II, and 31% and 22% for stage III. The difference

of DSS between the patients with stage II and stage III was statistically significant ( $P = 0.0016$ ). The CR rate and the 2- and 3-year DSS for the CRT group were 34%, 44%, 29%, respectively, and these results were better than those for the RT group of 24%, 43%, 19%, respectively, however, these differences observed were not statistically significant. The outcomes of the patients with CRT-DOC regimen resulted in almost the same as those of CRT-PT regimen group.

**Conclusion:** Our results revealed that definitive radiation therapy for squamous cell carcinoma of the esophagus is effective. Further investigations of the protocol of radiation therapy technique or chemotherapy are needed to clarify the impact of CRT on prognosis of the patients with this disease.

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### EGFR, p-Erk and p-AKT Expression in Barrett's Esophagus (BE): A Prospective Pilot Study

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**Purpose:** BE is a recognised precursor of esophageal adenocarcinoma (EA). However, the rate of progression of BE to adenocarcinoma is very low (0.5% per year). Identification of biomarkers that predict progression to dysplasia and adenocarcinoma is important. Epidermal growth factor receptor (EGFR) is activated in EA, which in turn cross activates the proliferative Erk and the antiapoptotic Akt pathways. Prospective data regarding the expression of these biomarkers in BE are scanty. We explored the expression of EGFR, p-Akt, and p-Erk in a prospective pilot study in patients with BE and BE with dysplasia.

**Methods:** 21 patients with BE, and 9 patients with BE with dysplasia were prospectively enrolled. Esophageal mucosal samples were obtained endoscopically in all cases. Uniform tissue processing and fixation techniques were applied. Immuno-histochemical staining for EGFR, p-Akt, and p-Erk was performed using validated techniques. Informed consent was obtained from all participating patients.

**Results:** EGFR expression was seen in all but one BE cases; 13 (61%) had strong positive expression. 18 BE cases (90%) showed positive expression of either p-Akt or p-Erk. There were total 9 cases of BE with either low grade (7) or high grade (2) dysplasia. 8 out of these 9 cases showed positive expression of p-Akt while p-Erk was expressed in all. Strong positive expression of p-Akt and p-Erk was noted in 4 and 3 cases of BE with dysplasia, respectively. Significant correlation was observed between p-Akt and p-Erk expression in the whole study cohort [Kendall's tau = 0.3591, ( $P = 0.0403$ )]. Due to the small sample size, no statistical correlation could be inferred between expression of EGFR, p-Akt, p-Erk and the presence of low or high grade dysplasia.

**Conclusion:** Association between p-Akt and p-Erk can lead to a survival and growth advantage for the affected premalignant cells. Whether this association leads to an aggressive course in BE or if this represents a pre-dysplastic change is unknown at this time. A larger study in BE patients with the above biomarkers is warranted.

Histology	EGFR + (++++)	p-Akt + (++++)	p-Erk + (++++)
BE (21)	20 (13)	18 (8)	20 (3)
Dysplasia (9)	9 (7)	8 (4)	9 (3)

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### Objective Documentation of the Link between Gastroesophageal Reflux Disease and Obesity

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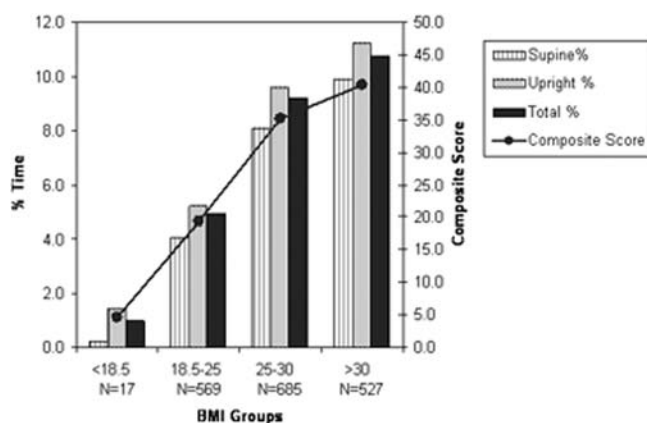
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**Purpose:** Obesity and gastroesophageal reflux disease (GERD) are important health epidemics. Previous studies have demonstrated that increasing body mass index (BMI) is associated with GERD symptoms, however, little is known about its relationship with objectively proven GERD. The aim of this study is to investigate the relationship between BMI and 24-hour esophageal pH.

**Methods:** A cross-sectional analysis of 1798 patients (49% male, mean age 51.3+/-14) referred for assessment of GERD symptoms between 1998 and 2006. Patients with previous foregut surgery and abnormal gastric pH were excluded. Esophageal manometry was performed to assess the lower esophageal sphincter (LES). Nasoesophageal 24-hour pH testing was done 5 cm above the upper border of the LES off medication. Patients were categorized by BMI [weight in kg/(height in m)<sup>2</sup>] according to World Health Organization classification (underweight < 18.5, normal 18.5–24.9, overweight 25–29.9, obese ≥ 30) for comparison of degree of acid exposure. A subgroup of patients with a competent LES (total length ≥ 2.7 cm, abdominal length ≥ 1.4 cm and resting pressure ≥ 5.1 mmHg) were also analyzed to eliminate the confounding effect of a defective valve. Kruskal-Wallis, Mann-Whitney, Chi-square and Spearman tests were used to assess statistical significance.

**Results:** The mean BMI was 27.8 (SD = 5.5). Compared to patients with a normal BMI, overweight patients have significantly more acid exposure (Figure) and a higher prevalence of a defective LES ( $P < 0.0001$ ), with a further increase among obese patients. Increasing BMI correlated with increasing composite score ( $r = 0.3$ ). To eliminate the confounding factor of a defective valve, the same analysis was performed limited to the group of patients with a competent LES. Similar associations between increasing BMI and degree of acid exposure and prevalence of defective LES were seen.

**Conclusion:** Increasing body mass index is associated with more severe objective indicators of GERD. This effect is independent of the presence of a defective valve.[figure1]



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#### Derivation and Validation of a Short Reflux Symptom Questionnaire (ReQuest in Practice<sup>TM</sup>) in Patients with GERD

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**Purpose:** ReQuest in Practice<sup>TM</sup> (RiP<sup>TM</sup>), a shortened form of the fully validated ReQuest<sup>TM</sup> questionnaire, was designed to allow patients' self-assessment of GERD symptoms in day-to-day clinical practice.

**Methods:** Data from previous studies showing a high correlation of symptom frequency  $\times$  intensity with resultant distress was used to devise an abbreviated questionnaire, RiP<sup>TM</sup>. Visual analogue scales were used to assess 5 symptom dimensions plus the patients' general well-being. Acid complaints, upper abdominal/stomach complaints, lower abdominal/digestive complaints, and nausea form the subscale RiP<sup>TM</sup>-GI; general well-being and sleep disturbance form the subscale RiP<sup>TM</sup>-WS.

120 patients with GERD were studied to determine the construct validity, internal consistency and the intra-class correlation coefficient (ICC) of RiP<sup>TM</sup>. Half the patients completed RiP<sup>TM</sup> followed by ReQuest<sup>TM</sup>. The other half completed the same questionnaires in reverse order to avoid a sequence bias. Before and after endoscopy all patients completed the health-related quality of life questionnaire GERDyzer<sup>TM</sup>.

A high Spearman correlation coefficient (SCC) of >0.75 of ReQuest<sup>TM</sup> and RiP<sup>TM</sup> would establish the applicability of all validation parameters of the former (Cronbach's alpha: 0.9; ICC: 0.86; test-retest reliability: 0.85; responsiveness index: 165.3) to the latter. Consequently, construct validity was assessed by correlating RiP<sup>TM</sup> with ReQuest<sup>TM</sup> and with GERDyzer<sup>TM</sup>. In addition, Cronbach's alpha and ICC were calculated directly for RiP<sup>TM</sup> and its subscales.

**Results:** The SCC of ReQuest in Practice<sup>TM</sup> and ReQuest<sup>TM</sup> was 0.9, indicating that the two are parallel forms. Internal consistency was high (Cronbach's alpha: 0.9) establishing the suitability of RiP<sup>TM</sup> to assess and monitor individual patients. Psychometric evaluation revealed an ICC of 0.99. The RiP<sup>TM</sup>-WS subscale correlated well with the different dimensions of GERDyzer<sup>TM</sup> (SCC: 0.65) and with the GERDyzer<sup>TM</sup> total score (SCC: 0.80).

**Conclusion:** ReQuest in Practice<sup>TM</sup> is a valid and reliable instrument for symptom assessment in GERD. It may be used by individual patients in day-to-day clinical practice and thus can potentially assist the physician in monitoring response to treatment.

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#### Effect of Obesity on Symptom Resolution in Patients with Gastroesophageal Reflux Disease (GERD)

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**Purpose:** To determine if body mass index (BMI) affects heartburn (HB) resolution in GERD patients, as obesity is reported to be associated with higher esophageal acid exposure and may impact treatment outcomes in GERD patients.

**Methods:** Data from 2 randomized, double-blind studies of similar design comparing esomeprazole 20 or 40 mg once daily with placebo (SH-QBE-0053 and -54) were pooled and analyzed. Patients were aged 18 to 75 y, had a history of HB for ≥6 months with symptoms on ≥4 of the last 7 d before study entry, and were negative for erosive esophagitis confirmed by endoscopy within 10 d of study entry. Patients returned daily HB diary cards at weeks 2 and 4. HB resolution was defined as recordings of none for HB symptoms for each of the last 7 d of the study on a scale of none, mild, moderate, severe. A Mantel-Haenszel  $\chi^2$  test (MHT) was conducted to test for an association of BMI category with baseline HB severity. Logistic regression models (LRMs) were fit with HB resolution as the dependent variable and BMI as a continuous independent variable. The LRMs adjusted for treatment, study, baseline HB severity, age, sex, race, *H pylori* result, and presence of hiatal hernia.

**Results:** In total, 704 patients with nonerosive reflux disease (NERD) were analyzed. There was no apparent relationship between baseline HB severity and BMI (MHT  $P = .2755$ ) (Table). The LRMs showed no significant effect of BMI on HB resolution ( $P = .9853$ ). The odds ratio estimate was 1.000 (95% CI, 0.972–1.030). No significant interactions with BMI and other variables were found.

**Conclusion:** In NERD patients, obesity had no apparent effect on baseline HB severity or on resolution of HB symptoms with PPI therapy. This

finding suggests that PPI dosing adjustments based on BMI may not be needed.

HB resolution rates by BMI

Baseline Severity	BMI	HB Resolution Rate (%)			
		N	Placebo	N	PPI
None	<25	13	7.7	16	31.3
	25 to <35	27	7.4	58	36.2
	≥35	11	9.1	11	45.5
Mild	<25	17	5.9	61	32.8
	25 to <35	52	19.2	97	30.9
	≥35	8	12.5	23	39.1
Moderate	<25	28	17.9	49	34.7
	25 to <35	45	15.6	83	44.6
	≥35	11	18.2	24	20.8
Severe	<25	8	0.0	11	72.7
	25 to <35	12	8.3	29	34.5
	≥35	6	0.0	4	25.0

\*Day before treatment or first day of treatment

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### Intragastric Acid Control in Patients Who Have Barrett's Esophagus: Comparison of Once- and Twice-Daily Regimens of Esomeprazole and Lansoprazole

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**Purpose:** To compare the efficacy of oral doses of once-daily (QD) and twice-daily (BID) esomeprazole and lansoprazole for the control of intragastric pH in patients who have Barrett's esophagus (BE).

**Methods:** In this multicenter, randomized, open-label, crossover study, the steady-state 24-hour intragastric pH profile was evaluated in adult patients who were negative for *Helicobacter pylori* infection and had histologically confirmed BE within 2 years of study entry. Patients were randomly assigned to crossover these 2 treatment arms: oral esomeprazole 40 mg QD followed by BID dosing or oral lansoprazole 30 mg QD followed by BID dosing. Study drug was taken 30 minutes before breakfast for QD dosing or 30 minutes before breakfast and dinner for BID dosing. On or after days 14 (QD) and 9 (BID) patients underwent a catheter-based 24-hour pH study. There was no washout period between doses; however, sufficient days preceded each 24-hour monitoring period to ensure washout of the previous drug and to reach steady-state levels of the next drug. The percentage of time that intragastric pH was >4 and the least-squares mean (LSM ± SEM) were calculated for each treatment from a mixed model ANOVA. Patients had to complete both comparative treatment sequences and have valid pH data to be included in the primary analysis population (per-protocol).

**Results:** Of 113 patients randomized, 46 (mean age, 58 years; men, 67%) provided evaluable pH data for the primary end point (QD comparison). The LSM overall time that pH was >4 was 16.0 hours for esomeprazole QD and 12.1 hours for lansoprazole QD ( $P < .0001$  vs esomeprazole) (see Table).

LSM (SEM)% time pH &gt;4 for QD and BID dosing of esomeprazole and lansoprazole in BE patients

Treatment	% Time pH >4	pH >4 for ≥12 h: n (%)
Eso 40 QD	66.9 (2.6)	40 (87)
Lanso 30 QD	50.6 (2.6)*	24 (52)
N = 46		
Eso 40 BID	81.2 (2.2)	40 (98)
Lanso 30 BID	64.3 (2.2)*	33 (80)
N = 41		

Eso, esomeprazole; Lanso, lansoprazole. \* $p < 0.0001$  (eso vs. lanso)

**Conclusion:** In BE patients, oral esomeprazole 40 mg QD provides greater control of intragastric acid at steady state than oral lansoprazole 30 mg QD. Esomeprazole 40 mg BID provided greater acid control versus lansoprazole 30 mg BID.

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### Tissue Ingrowth in a Fully Covered Self-Expandable Metallic Stent

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**Purpose:** Esophageal stents are being increasingly used in the management of esophageal leaks. Tissue ingrowth after insertion of a **partially** covered self-expanding metal stents (P-CSEMS) interferes with stent removal. This could be avoided by the use of **fully** covered self-expanding metal stents (F-CSEMS).

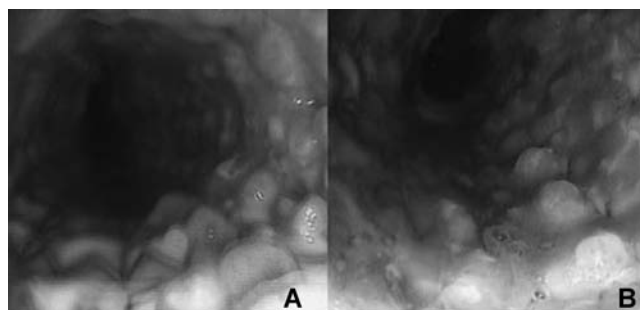
Despite the full covering, there is a potential risk of tissue ingrowth as observed in two patients at our center. Our objective is to present the cases with a description of the endoscopic removal of F-CSEMS with tissue ingrowth.

**Case 1:** A 57-year old male presented with spontaneous perforation of the distal esophagus. Emergent surgical repair failed and the esophageal leak recurred. EGD revealed a 1.5 cm perforation. A F-CSEMS -Alimaxx-E (22 mm × 120 mm, Alveolus, Inc, Charlotte, NC) was inserted. Contrast esophagography on day 6 revealed absence of free drainage of contrast into the stomach suggesting obstruction. EGD showed *extensive tissue ingrowth through the upper 2/3 of the stent* and a flap valve effect from the cardia. **Stent Removal:** The stent was loosened from the ingrowth at multiple locations with an Alligator forceps and was removed in one piece. A Polyflex stent (Boston Scientific Inc, Natick, MA) was inserted (*total time: 1.5 hours*); 7 weeks later, the stent was removed and the fistula healed.

**Case 2:** A 29 year old female developed esophageal leak after myotomy and epiphrenic diverticulectomy for achalasia. Due to migration of a Polyflex stent, repeat thoracotomy and surgical closure reinforced with diaphragmatic muscle was undertaken, without success. Insertion of a F-CSEMS (Alimaxx-E stent) closed the leak. EGD two weeks later revealed *severe tissue ingrowth in the distal third of the stent*.

**Stent Removal:** When the spine of the stent was pulled with an Alligator forceps, the free portion of the stent fractured leaving the portion with ingrowth in-situ. An overtube was used and the stent removed in a piece-meal fashion (*total time: 3 hours*). The fistula healed successfully.

**Conclusions:** Tissue ingrowth is a potential complication even in F-CSEMS. Tissue ingrowth could pose a technical challenge at endoscopic removal of these stents. One should be prepared to manage this complication.[figure1]



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### Insulin-Like Growth Factor-1 Pathway Activation in Barrett's Esophagus

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**Purpose:** Barrett's esophagus (BE) is associated with obesity independent of GERD. We hypothesized that increased insulin levels associated with obesity and insulin resistance might lead to cell proliferation via the insulin-like growth factor -1 (IGF-1) cell signaling pathway.

**Methods:** Fasting serum insulin levels and glucose levels were measured in 14 BE subjects. Immunohistochemistry (IHC) was performed on paraffin-embedded tissue from 14 BE cases using antibodies to phosphorylated-AKT and phosphorylated-mTOR, cell signaling molecules known to be phosphorylated intermediates in the insulin – IGF signaling pathway.

**Results:** IHC with Ki-67, a cellular proliferation marker, correlated strongly with phosphorylated-AKT as well as phosphorylated-mTOR immunostaining intensity in BE. Strong immunostaining for phos-AKT and phos-mTOR was present in 8 specimens. Immunostaining was generally weak in the other 6 specimens. All 3 of the BE subjects with insulin resistance, as calculated by the homeostasis model (HOMA-IR > 3.8), showed strong immunostaining of phos-AKT and phos-mTOR. Six subjects with HOMA-IR > 3 also showed strong immunostaining. Only 2 subjects with HOMA-IR < 3 showed strong immunostaining whereas the other 6 with low HOMA-IR showed weak immunostaining. The non-BE columnar epithelium as well as the squamous epithelium showed negligible immunostaining.

**Conclusion:** These preliminary results support our hypothesis that insulin and IGF-1 may act as growth factors for Barrett's epithelium through phosphorylated AKT and m-TOR intermediates.

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### Does Combined Multichannel Intraluminal Esophageal Impedance and Manometry Predict Postoperative Dysphagia after Laparoscopic Nissen Fundoplication?

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**Purpose:** The purpose of this study was to identify if the addition of multichannel intraluminal esophageal impedance (MII) to manometry may detect those patients most at risk of developing postoperative dysphagia.

**Methods:** Between March 2003 and April 2006, 69 patients who agreed to participate in this study were prospectively enrolled. All patients completed a pre-operative symptom questionnaire, MII/manometry, and 24-hour pH monitoring. Symptom questionnaires were administered post-operatively at a median of 18 months (range: 6–46 months), and we defined dysphagia (both preoperative and postoperative) as occurring more often than once a month with a symptom severity score (SSI – scale = 0–10)  $\geq 4$ . LNF was performed in all cases.

**Results:** Thirty patients (43%) reported pre-operative dysphagia. There was no significant difference in pH monitoring, lower esophageal sphincter (LES) pressure/relaxation, peristalsis, liquid or viscous bolus transit, or bolus transit time between patients with and without pre-op dysphagia. In those patients reporting preoperative dysphagia, the severity of dysphagia improved sig-

nificantly from  $6.8 \pm 2$  to  $2.6 \pm 3.4$  ( $P < .001$ ) after LNF. Twelve (17%) patients reported dysphagia postoperatively. Patients with post-op dysphagia had similar LES pressure and relaxation, peristalsis, and esophageal clearance to those without dysphagia. The only predictor of post-operative dysphagia was the presence of pre-operative dysphagia (Table).

**Conclusion:** Neither MII nor manometry are effective in predicting dysphagia before or after laparoscopic Nissen fundoplication. The presence of dysphagia preoperatively is the only predictor of dysphagia after the operation.

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### Esophageal Capsule Endoscopy for Evaluation of Gastroesophageal Reflux Disease

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**Purpose:** Esophagogastroduodenoscopy (EGD) is commonly used to evaluate suspected or established gastroesophageal reflux disease (GERD). Esophageal capsule endoscopy (ECE) may offer an alternative approach to visualize esophageal lesions commonly associated with GERD. The objective of this study was to report the ECE findings and complication rate in a large series of patients with GERD-like symptoms.

**Methods:** From April 2005-June 2007, a total of 312 ECE were performed in patients with GERD symptoms. ECE findings deemed consistent with reflux esophagitis (hyperemia, erosions, ulceration, strictures, Barrett's esophagus) were graded using the modified 1–5 scale Savary-Miller classification. The esophagogastric junction (GEJ) was carefully examined for the hiatal hernias, Schatzki's rings, and strictures.

**Results:** Eight (2.6%) of 312 ECE cases remained in the esophagus for the entire imaging time ( $\geq 20$  minutes). In one case (0.3%), no esophageal images were recorded due to rapid esophageal transit. The mean esophageal transit time was  $138.0 \pm 232.2$  seconds (excluding 8 cases in which the ECE did not leave the esophagus). Reflux esophagitis was diagnosed in 194 patients (62.2%): Savary-Miller classification – Grade 1 (N = 121), Grade 2 (N = 62), Grade 3 (N = 8), Grade 4 (N = 1) and Grade 5 (N = 2). One hundred forty-four patients (46.2%) had hiatal hernia. Eight cases (2.6%) had Schatzki's ring. We identified seven cases (2.2%) with suspected Barrett's esophagus, six (1.9%) with irregular Z line, and one (0.3%) with small islands of pinkish mucosa. Incidental gastric mucosal findings included: gastric erosions (N = 37), redness/submucosal hemorrhage (N = 5), gastric ulceration (N = 4), gastric nodularity/polyps (N = 2). No esophageal strictures, ECE impaction, or other complications occurred in this case series.

**Conclusion:** From these data, ECE was a safe and easy non-invasive technique to evaluate the esophageal mucosa in patients with GERD symptoms.

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### PillCam ESO for Evaluating the Esophagus in the Workplace: Making It Even Easier To Swallow

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**Purpose:** Increasing use of over-the-counter acid suppression medications, fear of the procedures, requiring an escort, and concerns about loss of productivity in the workplace are barriers to undergoing thorough evaluation for chronic or intractable reflux symptoms. Capsule endoscopy, specifically PillCam ESO and the Rapid Access real-time viewer, were welcomed into a workplace and performed on 10 non-sedated employees during their work day, saving time and maintaining worker productivity.

This pilot study was performed at a large self insured Boston based company with about 4000 employees. Employees have access to an internal medicine, primary care practice on site. Two physicians screened patient/employees over a couple of months to identify patients with persistent reflux symptoms. Patients were excluded if they had a history of other unexplained

Pre-operative findings	Post-operative dysphagia (N = 12)	No post-operative dysphagia (N = 57)	P-value
LESP (mmHg)	20.4 $\pm$ 12.4	13.7 $\pm$ 10.7	.354
% peristalsis	80 $\pm$ 32	88 $\pm$ 18	.685
% LBT	78 $\pm$ 30	79 $\pm$ 24	1.000
Liquid BTT (sec)	6.4 $\pm$ 1.4	7.0 $\pm$ 1.4	.838
% VBT	66 $\pm$ 33	64 $\pm$ 29	.526
Viscous BTT (sec)	7.4 $\pm$ 2	7.8 $\pm$ 2	.561
% time pH < 4	13.2 $\pm$ 9.4	11.3 $\pm$ 11.9	.602
DeMeester score	52.3 $\pm$ 38.4	40 $\pm$ 40.1	.358
Pre-op dysphagia (n)	9/12 (75%)	21/57 (37%)	<.001

gastrointestinal symptoms, previous bowel surgery, obstructive symptoms, an implantable electromedical device or pregnancy. A single gastroenterologist with experience with capsule endoscopy performed the procedures on site. Ten patients were identified, ages 36 to 65, where there was 5 males and 5 females. All patients were full time working employees.

On two separate occasions, a total of 10 PillCam ESO studies were performed. Results included eight patients with normal mucosa. Two patients underwent a subsequent EGD. One patient had gross findings suggestive of Barrett's esophagus, later proven by biopsy. A second patient had gross evidence suggesting reflux esophagitis, but an incomplete visualization of the Z-line limited the study. The first 5 patients were interviewed, ingested the capsule, and received their results by consultation with the gastroenterologist in a total of a 3 hour session. The next 5 patients were evaluated using the real-time viewer. For this latter group of 5 patients, the entire process was shortened to less than 40 minutes from ingestion to consultation and reporting.

PillCam studies performed at the workplace at a large self-insured company safeguarded worker productivity and provided state-of-the-art medical care for patients with chronic reflux symptoms. Future PillCam studies, not just to evaluate the esophagus, could be started at the work site with capsule ingestion and being more convenient for the patient.

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#### Are There Any Motility Disturbances in Eosinophilic Esophagitis?

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**Purpose:** To identify manometric patterns of the esophagus in a series of patients with eosinophilic esophagitis (EE) in an effort to explain any motility contributions to their dysphagia.

**Methods:** 10 patients (9 males) with EE (>20 eosinophils/hpf on the proximal esophageal biopsy) underwent manometric evaluation of the esophagus using the water perfused catheter system. The criteria for a normal esophageal manometry (EM) exam were: a) Lower esophageal sphincter (LES) pressure of 15–35 mmHg, and b)  $\geq 80\%$  of contractions being peristaltic after wet swallows, with a normal range of contraction amplitude between 50–150 mmHg. Demographic data and clinical history for each of these patients was also obtained.

**Results:** Mean age of the patients was 32 years (Range: 14–51). Intermittent non-progressive dysphagia was the main presenting complaint, while one also had an acute food impaction. One patient had food allergies, 6 patients had other allergic manifestations of either allergic rhinitis, or bronchial asthma. Six patients were on proton pump inhibitors (PPI) for gastro esophageal reflux disease (GERD) symptoms. On EM – two patients had low amplitude (<30 mmHg), non-peristaltic contractions; one in the mid-esophageal segment, while the other was more diffuse with 30% of the contractions being non-peristaltic after wet swallows. Four patients had decreased LES pressure (<15 mmHg) and they were receiving PPI's. One patient had 20% of contractions reaching "nutcracker" criteria (>200 mmHg). The remaining 3 patients had a normal manometric evaluation.

**Conclusion:** 1) Although EE is not associated with a specific manometric pattern to explain the dysphagia, 20% of patients did have a major motor disturbance in the smooth muscle function. 2) EE can co-exist with GERD, but PPI therapy alone does not improve the dysphagia. 3) There should be a high index of suspicion for EE when dysphagia is not being explained by esophageal manometry, endoscopy, or imaging studies.

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#### A New Surgical Approach to Gastroesophageal Reflux Disease: Nissen Fundoplication with Highly Selective Vagotomy

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**Purpose:** A standard Nissen fundoplication does not address gastric acid secretion; hence an accompanying highly selective vagotomy (HSV), which will reduce gastric acid secretion by 60%, could help sustain long-term symptom response. To assess this we measured the rate of proton-pump inhibitor (PPI) use postoperatively in a cohort of patients with gastroesophageal reflux disease (GERD) who underwent Nissen fundoplication with HSV in comparison to a group who did not undergo HSV during the procedure.

**Methods:** 14 patients (8 females) underwent a Nissen fundoplication with HSV, and 19 without HSV for refractory GERD symptoms, particularly nocturnal regurgitation. PPI use pre-operatively and during the postoperative follow up was recorded. Esophageal manometry, esophageal pH monitoring, and gastric emptying scintigraphy (GES) were performed preoperatively.

**Results:** Mean age of patients in both the groups was similar at 47 years. The mean lower esophageal sphincter pressure was 8 mmHg (95% CI: 6–10 mmHg) in the HSV and was not significantly different ( $P=0.44$ ) than the non-HSV group (Mean 10 mmHg; 95% CI: 9–11 mmHg). The mean% of retained food after 4 hours on GES was also similar ( $P=0.44$ ) in both groups: 8% (95% CI: 2–14%) in the HSV group and 12% (95% CI: 5–19) in the non-HSV group. All patients in both groups were on a PPI (Usually double dose therapy) prior to the surgery. Median duration of follow up was 63 months (Range: 6–88 months). 1/14 (7%) patients in the HSV group and 9/19 (47%) in the non-HSV group either remained on a PPI post-operatively or were re-started, generally within the first 6 months after surgery. The odds ratio of being on a PPI in the HSV group after surgery as opposed to the non-HSV group was 0.08 (95% CI: 0.009–0.8). None of the patients in the HSV group had symptoms suggestive of gastroparesis postoperatively.

**Conclusion:** 1) Adding a HSV to the standard Nissen fundoplication procedure significantly reduced the use of PPI's during long term post-operative follow up and was not associated with any adverse events. 2) This new surgical approach for refractory GERD warrants further objective studies to confirm these important observations.

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#### GERD – Maintenance Therapy with PPI v/s “Pre-Emptive Use of PPI”

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**Purpose:** GERD is one of the common indication to see a gastroenterologist. Due to its prevalence, the economic impact of management of GERD is huge when the endoscopy, initial induction therapy followed by tapering dose and then maintenance therapy.

The idea of this presentation is to check if we can generate consensus about “Pre-emptive use of PPI” to reduce recurrence compared to maintenance therapy. When the patient can recall the event or meal that caused first recurrence of GERD while they were off, were advised “Pre-emptive use of PPI”-meaning taking PPI 30 to 60 minute before the precipitating event. During my search, no study has been published that evaluated this way of treatment.

**Methods:** During four years, 40 patients with endoscopically proven GERD were followed in office. Due to severity and duration of symptoms, they all had Endoscopic evaluation with biopsy. Those who had Barrett's esophagus were excluded to begin with. The others were followed over period of four years with long-term maintenance with PPI v/s “Pre-emptive use of PPI”. Those patients who had economic reason, or denial by insurance or safety concern over the long-term use of conventional maintenance therapy were assigned to “Pre-emptive use of PPI” group.

**Results:** Many patients, who had recurrence of GERD, were able to predict the event like heavy meal over weekend or social gathering or drinking alcohol. When they are given “Pre-emptive Therapy with PPI before the event, the incidence of recurrence of GERD was much reduced compared to no use at all. Not only that it was comparable to the group of patient who had chronic maintenance therapy with PPI.

**Conclusion:** “Pre-emptive use of PPI” reduces number of recurrence of GERD in patients who had predictable culprit event. Not only that it was comparable to chronic long-term maintenance therapy, but also the cost is probably one forth to one fifth. (As most of the patient needed it once or twice a week compared to seven days week).

The strategy of “Pre-emptive use of PPI” can cause significant cost containment and saving and it worth exploring at larger scale.

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### Changes in Quality of Life over Time in Patients Registered on the Mayo Clinic Esophageal Adenocarcinoma and Barrett's Esophagus Registry

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**Purpose:** To explore the change in patient quality of life (QOL) over time in patients with esophageal adenocarcinoma (EA) or Barrett's esophagus (BE).

**Methods:** Members of the Mayo Clinic EABE Registry completing two QOL assessments (baseline and 1 year (range 11–16 mos)) were selected to evaluate whether QOL changes occurred over time. Completed was the Linear Analogue Self Assessment (LASA) containing 12 questions relating to QOL (overall, social, spiritual, physical, mental, emotional, social support, financial, pain, fatigue and legal issues). Each LASA question has a value from 0 (worst) to 10 (best). The change from baseline was calculated for each question. Further, the change in each score was dichotomously categorized as being a positive (increase in QOL) or negative (decrease in QOL) change. Basic summary statistics were computed for baseline characteristics and QOL scores. Student's t-tests were used to determine significance in changes from baseline, Kruskal-Wallis tests were performed for the difference in continuous data between groups and Fischer-Exact tests were performed for differences in categorical data between groups.

**Results:** Data from 372 patients was analyzed. Median age was 66 (range 30–93). 81% were male, 10% received treatment for EA prior to QOL assessment, 8% received treatment between assessments, and 82% received no treatment. Change in scores showed that the group had significant decreases in pain frequency ( $<0.001$ ) and social support ( $<0.001$ ) and a marginally significant decrease in pain severity ( $P = 0.06$ ). Patients treated between assessments had a higher change in financial well-being score than the other two groups (mean 1.5 vs  $-0.1$  vs  $-0.1$ ,  $P=0.001$ ) and a higher change in legal well-being (mean 0.9 vs  $-0.1$  vs  $-0.1$ ,  $P = 0.04$ ). Treated patients reported higher pain severity ( $P = 0.048$ ). There were no differences in the change from baseline scores between gender or age groups. The categorical change resulted in a difference in financial well-being ( $P = 0.03$ ) and social support ( $P = 0.03$ ). Differences in physical well-being were marginal ( $P = 0.06$ ).

**Conclusion:** Treated patients had less financial concerns and legal concerns but did experience higher pain severity. The significant change from baseline of social support was not evident upon subgroup analyses.

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### Decreased GLIPR1 Expression in Esophageal Adenocarcinoma

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**Purpose:** To determine whether GLIPR1 may be altered in esophageal adenocarcinoma (ACA).

**Methods:** Sections from esophagectomy specimens including 13 with Barrett's metaplasia negative for dysplasia (BMND) and 22 adenocarcinomas (ACA) were stained for the GLIPR1 protein using the immunohistochemistry (IHC). The percentage of positive cells was scored on a scale of 0–5

with 0 completely negative; 1, 1–10%; 2, 11–25%; 3, 26–50%; 4, 51–75%; and 5,  $>75\%$  of the cells positive. The intensity of staining was scored as 0, completely negative; 1, weak; 2, moderate; and 3, strong intensity. Paired frozen samples of 4 normal and ACA were assayed for GLIPR1 promoter hypermethylation using the bisulfite method.

**Results:** Staining was both nuclear and cytoplasmic, and was completely abolished by preincubating the antibody with the immunizing peptide. The immunostaining score (IC) score for the BMND cases ranged from 6–15, whereas the score for ACA ranged from 0–10 with 4 of the ACA cases completely negative and 14 having very low IC scores (0–2). The mean IC score for the ACA, 3.3, was significantly lower than that for BMND, 11, ( $P < 0.0001$ , unpaired t-test). In a smaller subset of the cases in which both BMND and ACA were from the same esophagectomy specimens, the mean IC score for ACA (4.5) and BMND (10.9) were also significantly different ( $P = 0.0105$ , paired t-test). The methylation status of the gene did not correlate with the levels of protein, as determined by IHC, in paired samples of normal and tumor tissues.

**Conclusion:** We conclude that the majority of esophageal adenocarcinomas have significant reduction of GLIPR1 protein expression suggesting that GLIPR1 plays a significant role in malignant transformation in Barrett's esophagus.

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### ADHERE Study: Application of Dx-pH Catheters in the Evaluation of Patients without Gastroesophageal Reflux Disease (GERD)

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**Purpose:** The Restech Dx-pH probe is a new ambulatory pH monitoring device which uses a sensitive sensor to capture liquid and aerosolized acid. Its design allows for convenient placement in the oropharynx above the upper esophageal sphincter (UES) without the need for manometry or endoscopy. Currently, no normative data for this device exists nor has its application been validated for use in patients with GERD or extraesophageal symptoms. Our aim was to provide data for Dx-pH probes in the oropharyngeal and distal esophageal sites in normal subjects.

**Methods:** Normal subjects underwent prolonged ambulatory Dx-pH testing in the oropharynx and distal esophagus. The distal probe was placed 5 cm above the manometrically measured LES, and the proximal probe was placed visually into the oropharynx at the level of the uvula at a known distance from the UES. The following reflux parameters were measured using the Mann-Whitney non-parametric procedure: median% time below pH 4, 5, and 6, as well as, mean number of events per 24 hours below each of the above pH cutoffs.

**Results:** A total of 31 normal subjects (11 M/20 F); mean age 33.2 yrs (range 21–56) comprised the study population. The median (95th percentile) total% time below pH 4, 5, and 6 in the distal esophagus was 1.0 (5.3), 2.9 (12.6), and 10.4 (46.1), respectively (Table 1). For the oropharyngeal proximal probe, the median (95th percentile)% time below pH 4, 5, and 6 was 0.0 (0.0), 0.0 (2.4), and 1.0 (22.5), respectively. Finally, for the proximal probe, the median (95th percentile) number of events below pH 4, 5, and 6 was 0.0 (0.6), 0.0 (8.4), and 4.1 (197.5), respectively, over a 24 hour period in this normal population.

**Table 1.** Median Dx-pH probe measurements: oropharynx vs. esophagus

Parameters	Oropharynx (25–75%)	Esophagus (25–75%)
% Time pH < 4	0.0 (0.0–0.0)	1.0 (0.4–3.5)
# of events/24 hrs < pH 4	0.0 (0.0–0.0)	
% Time pH < 5	0.0 (0.0–0.0)	2.9 (1.3–6.6)
# of events/24 hrs < pH 5	0.0 (0.0–0.0)	
% Time pH < 6	1.0 (0.0–11.2)	10.4 (5.2–20.4)
# of events/24 hrs < pH 6	4.1 (0.0–56.9)	

**Conclusion:** The normative values for the new Dx-pH catheter probe compares favorably to the accepted gold standard pH monitoring device. Future studies can focus on comparative evaluations between patients with and without GERD using the Dx-pH catheter probe.

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### Coexistence of Barrett's Esophagus and Eosinophilic Esophagitis

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**Purpose:** The interaction between gastroesophageal reflux (GERD) and eosinophilic esophagitis (EoE) is complex. There is a high prevalence of GERD symptoms in patients with EoE. Patients with GERD have increased eosinophils in the esophageal epithelium. EoE may cause exudates and strictures but it is unclear whether complications such as Barrett's esophagus occur in EoE. Purpose: 1. Determine the prevalence of Barrett Esophagus (BE) in patients with Eosinophilic esophagitis (EoE). 2. Compare the demographic, clinical and endoscopic features of patients with EoE to those with EoE and BE.

**Methods:** Retrospective review of our series of consecutive patients with EoE (N = 71) evaluated in the last year. EoE was diagnosed if >20 E/HPF were identified. BE was diagnosed when "salmon-like" epithelium was seen in the tubular esophagus and biopsy confirmed intestinal metaplasia.

**Results:** Barrett's esophagus was found in 14% (10/71) patients with EoE. Six had long segment BE ( $\geq 3$  cm) and 4 a short segment BE. Demographics, clinical and endoscopic features are summarized below:

**Conclusion:** BE coexists in 14% of patients with EoE. Endoscopists should be aware of the potential occurrence of these two common disorders on the same patient. Esophageal symptoms of GERD and dysphagia overlap in these patients. Subjects with BE and EoE are more likely to have GERD symptoms and hiatus hernia while those with EoE without BE are more likely to have dysphagia and rings. A substantive proportion of patients with BE and EoE has peripheral eosinophilia and allergies. Further studies are needed to determine the potential interactions between these two common entities.

Demographics and Symptoms

Disorder	N Cases	Mean Age (range)	White race	GERD	Dysphagia	Food impaction
EoE + BE	10	58 (18-88)	9 (90%)	9 (90%)	6 (60%)	2 (20%)
EoE - BE	61	51 (19-71)	40 (66%)	31 (51%)	49 (80%)	20 (33%)

Endoscopic Findings, History of Allergies and Eosinophilia

Disorder	Hiatus Hernia	Rings	Furrows	White lesions	Distal Ring	Periph Eosinophilia	Allergies
EoE + BE N = 10	9 (90%)	4 (40%)	4 (40%)	2 (20%)	4 (40%)	7 (70%)	6 (60%)
EoE - BE N = 61	22 (36%)	37 (61%)	15 (25%)	13 (21%)	19 (31%)	17 (35%)	31 (51%)

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### Adenocarcinoma of Esophagus and Cardioresophageal Junction (CEJ): 10 Year Experience

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**Purpose:** Adenocarcinoma (AdenoCA) of the esophagus and CEJ has been on the rise in the Western population. To determine the outcomes, and predictors of survival in patients diagnosed with esophageal and CEJ AdenoCA.

**Methods:** The endoscopic database of patients undergoing EGD were retrospectively reviewed and analyzed for patients diagnosed with esophageal and CEJ AdenoCA. Treatment modalities (none, Chemo/XRT, surgery, and

stent placement), their complications, and survival rates for each cancer stage were obtained. Setting: VA medical center. Study period: 1997-2006. Statistics: Survival analysis with Kaplan Meier curves, Cox regression, and Chi square.

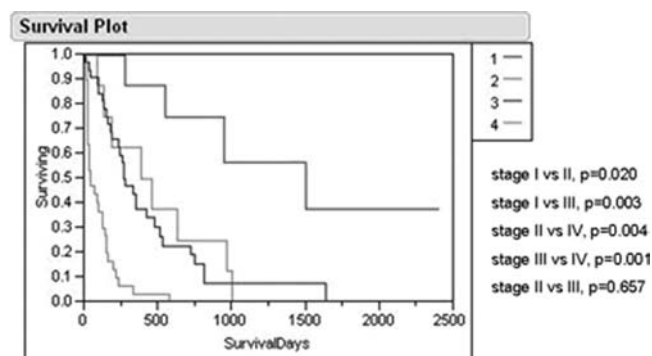
**Results:** There were 78 patients with esophageal AdenoCA and/or CEJ. The average prevalence per year was 0.49%. Only 4 patients had EGDs prior to diagnosis of AdenoCA with an incidence rate of 0.36%. The majority of patients were diagnosed as de novo AdenoCA. The mean age at diagnosis or stage did not vary over time.

From 1997 to 1999, up to 47.7% of patients were surgically treated; thereafter this decreased to 19% while Chemo/XRT increased to 45%.

Early stage detection of esophageal and CEJ adenocarcinoma did not improve over time. Staging, chemo/xrt, and year of diagnosis were all independent predictors of improved survival. For every year since diagnosis was made, the survival rate was 13.1% better. Chemo/XRT vs all other treatment options had a 50% better survival. The survival curves for each stage are shown in the Figure.

The complication rate for esophageal stents was significantly lower (16.6%) than surgery 60.7% (peri-operatively 47.7%, anastomotic stricture 13%) ( $P < 0.005$ ). All other comparisons among treatment options were not significant. Tumor recurrence after surgery was seen in one-third of patients (7/23).

**Conclusion:** 1) There was no change in the incidence or early detection of AdenoCA over time. 2) Most presentations are de novo and have advanced disease. 3) There has been a shift in treatment modalities over the study period. 4) Survival was dependent on staging and treatment modality chosen.[figure1]



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### Clinical Utility of the Bravo Capsule

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**Purpose:** The Bravo capsule is widely used to evaluate patients (Pts) with acid reflux symptoms. A preliminary study (Dukowicz et al. *Am J Gastroenterol* 2006; 101(9) Suppl:S48) appears to show it to be clinically useful. Our aim was to prospectively evaluate the clinical utility of the Bravo capsule in a large series of Pts by determining whether it changes diagnosis, provides new information, or alters management.

**Methods:** Prior to Bravo capsule deployment, referring physicians completed a questionnaire requesting: indications for the test; symptoms; prior testing; and medication use. Demographic information was obtained from the Pt. Patients were studied either on or off acid-suppressing medications. Two weeks after the referring physician received the results of the test a follow-up questionnaire was sent asking whether the Bravo capsule provided new information, and whether test results changed the Pt's diagnosis or management.



**Results:** During a 14 month period, 598 Bravo capsule studies were performed; 550 were available for inclusion. 308 fully completed questionnaires were returned (56%) and are the basis for this analysis. The mean age ( $\pm$ SD) at time of Bravo placement was 48 ( $\pm$ 16 years), 65% were women, and nearly all (97%) were Caucasian. The average age of symptom onset was 40 years ( $\pm$ 15), and average duration of symptoms was 72 months. The most common primary symptom was acid reflux (heartburn/regurgitation; 65%), followed by chest pain (8%), chronic cough (7%), dysphagia (6%), & ENT symptoms (4%). 92% of Pts had undergone prior testing, including EGD, barium swallow, and/or chest x-rays. 22% had undergone a previous pH test (either pH catheter or Bravo), and 65% of these studies were abnormal. Bravo capsule results provided new information in 72% of Pts, changed the diagnosis in 22%, and altered management in 58%. Management changes included: referral to surgery (26%), stopping a prior medication (15%), increasing the dose of a prior medication (15%), starting a new medication (11%) and other (33%).

**Conclusion:** This prospective study confirms and extends our preliminary results showing that the Bravo capsule is a clinically useful test. Future studies should be performed to define which Pt population will benefit most from Bravo capsule testing, and whether changes in management lead to improved patient outcomes.

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#### Dx-pH Monitoring: How Does It Compare to the Standard pH Probe?

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**Purpose:** Physiologic assessment of esophageal acid exposure is often performed utilizing ambulatory pH monitoring. Recently ambulatory Restech Dx- H probe is designed to record pH changes in the oropharynx in patients with suspected extraesophageal reflux symptoms. However, there are no validations of this instrument against the current standards in clinical practice. Thus, we aimed to compare the internal consistency of the new distal esophageal Dx-pH probe with the standard of care Sandhill pH probe.

**Methods:** Patients diagnosed with GERD (esophagitis at endoscopy or prior abnormal pH findings off acid suppressive therapy) underwent simultaneous ambulatory esophageal pH monitoring. The Dx-pH and Sandhill pH probes were positioned at 5 cm above the manometrically measured LES in each patient. Based on the inherent property of the devices, Dx-pH monitor recorded esophageal acid exposure every 0.5 seconds compared to a 5 second interval for the Sandhill probes. Outcomes assessed included episodes below pH 6, pH 5, and pH 4 and % time below pH 4, 5, and 6. The # times that pH fell below the cutoff was manually and electronically measured. The values were compared using the Wilcoxon signed rank test on the differences in the paired data.

**Results:** A total of 11 patients (5 male and 6 female) with mean (range) age of 40.9 (21–59) constituted the study population. 72.7% and 45.4% of the patients were complaining of daily heartburn and regurgitation, respectively. No statistically significant ( $P < 0.05$ ) differences were found between the Dx-pH and Sandhill devices for the number of times pH  $< 4$ , pH  $< 5$ , or pH  $< 6$ . The Dx-pH probe spent consistently more time at pH  $< 4$  ( $P = 0.131$ ), pH  $< 5$  ( $P = 0.049$ ), and pH  $< 6$  ( $P = 0.01$ ) than the Sandhill probe (Table 1).

Dx-pH catheter vs Sanhill probe performance at different pH cut offs.

Outcomes	Restech (25%–75%)	Sandhill (25%–75%)	P Value
# Events pH $< 4$	37 (20–53)	34 (17–60)	0.31
% Times pH $< 4$	8.0 (1–15)	6.0 (1–10)	0.13
# Events pH $< 5$	40 (18–55)	46 (31–62)	0.09
% Times pH $< 5$	14.0 (2–29)	13.0 (1–24)	0.04
# Events pH $< 6$	36 (9–62)	41 (15–47)	0.32
% Times pH $< 6$	43.0 (12–56)	23.0 (6–43)	0.01

**Conclusion:** Dx-probe identifies reflux events in the distal esophagus similar to current standard pH catheter but it has less variability. The clinical potential of this diagnostic device will need to be tested in patients with extraesophageal GERD.

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#### The Effect and Timing of Food on the Pharmacokinetics and Pharmacodynamics of TAK-390MR (Modified Release): Evidence for Dosing Flexibility

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**Purpose:** TAK-390MR is a proton pump inhibitor that employs a modified release technology designed to provide prolonged plasma concentrations of TAK-390 following once daily oral dosing. This study evaluated the effect and timing of food on the pharmacokinetics (PK) and pharmacodynamics (PD) of TAK-390 after a single 90 mg dose of TAK-390MR.

**Methods:** Phase 1, open-label, single-dose, randomized, 4-way crossover study. Forty-eight healthy subjects (18–55 years) received a single oral dose of TAK-390MR 90 mg in the fasted state (A) and 3 fed states (30 minutes after the start of a high-fat breakfast [B], 5 and 30 minutes before a high-fat breakfast [C, D]). Serial blood samples were obtained for up to 24 hours postdose. To adjust for the effect of food on pH, baseline as well as postdose 24-h intragastric pH monitoring was performed for each regimen. Plasma concentrations of TAK-390 were determined using a validated LC-MS/MS assay; PK parameters were estimated using noncompartmental methods. PD parameters were calculated as the mean pH and % time pH  $> 4$  over 24-h. The effect of food and the timing of food on TAK-390 PK and PD were assessed and pairwise comparisons were conducted between the fasting and fed regimens. The 90% confidence intervals (CI) for relative bioavailability between 2 regimens were computed and a conclusion of no difference was made if the 90% CI for the ratios of TAK-390  $C_{max}$  and AUCs from 2 regimens were within 0.80 and 1.25. Changes in PD parameters from baseline to postdose were also assessed and pairwise comparisons between the fed regimens to the fasting regimen were also performed, with a test deemed statistically significant if the  $P$ -value was  $\leq 0.05$ .

**Results:** Forty-six subjects completed all regimens. TAK-390MR given under 3 fed conditions resulted in a modest and statistically significant increase in  $C_{max}$  and AUCs (9–31%) relative to fasting. No statistically significant difference for mean intragastric pH was observed among the dosing regimens in change from baseline over the total 24-h postdose interval. Although a statistically significant greater change from baseline was seen in % time pH  $> 4$  for both regimens A and D compared to regimen B, the small differences are not likely to be relevant.

**Conclusion:** Although TAK-390MR administered under various fed conditions compared to the fasted state had a statistically significant effect on the PK of TAK-390, the intragastric pH results indicate that TAK-390MR can be administered without regard to food.

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#### Eosinophilic Esophagitis/Ringed Esophagus: The Diagnostic Conundrum

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**Purpose:** Eosinophilic esophagitis (EoE) is defined classically as  $>20$  eos/HPF on esophageal biopsies. Common characteristics in EoE are dysphagia with associated rings/furrows seen on endoscopy. To date, no one has determined whether all rings seen on EGD represent EoE histologically or whether all EoE patients have the classical endoscopic findings of rings/furrows. This study was designed to correlate endoscopic findings and histology in EoE.

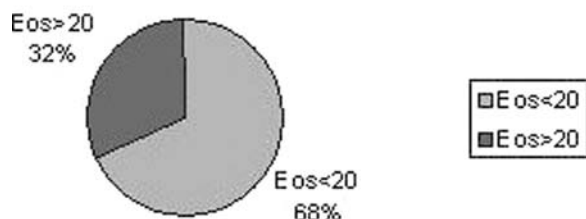
**Methods:** A retrospective analysis of all EGD's performed at the University for dysphagia in 2006 was performed. Per routine protocol, all cases were biopsied and evaluated for eosinophils. Patients with endoscopic findings of ringed/furrowed esophagus were identified. Cases were evaluated for evidence of EoE based on histologic criteria of  $>20$  eos/HPF.

All cases of histologically defined EoE were identified and grouped by their endoscopic findings as ringed/furrowed, normal, esophagitis, schatzki ring, or stricture.

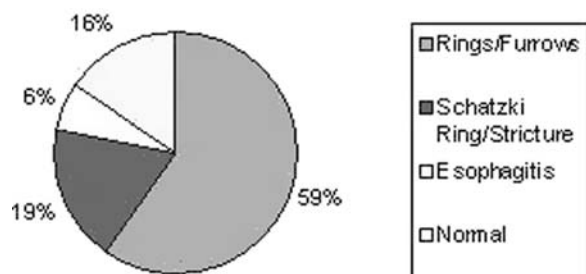
**Results:** Ringed esophagus was identified endoscopically in 28 patients (75% male, ave age 41 y). 19/28 (67.9%) met histologic criteria for EoE (graph). In the remaining patients, distal eosinophil counts averaged 2.5/HPF while proximal eos averaged 8.2/HPF. 32 patients met histologic criteria for EoE (62.5% male, ave age 42 y). 19/32 (59%) presented with endoscopic "rings or furrows." 13/32 (41%) had other endoscopic findings (graph).

**Conclusion:** EoE may present as a variety of phenotypes. Strictly adhering to histologic criteria for the diagnosis may result in an under-diagnosis as eosinophilic infiltration is patchy and likely sporadic. Gastroenterologists should have a high index of suspicion for EoE in any young patient who presents with dysphagia as endoscopy may not portray classical rings/furrows. Routine biopsies in this population are warranted.[figure1][figure2]

### Patients with Ringed Esophagus



### Endoscopic Findings in EoE



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### An Unusual Case of Esophageal Varices and Esophageal Dysmotility in a Healthy Young Female

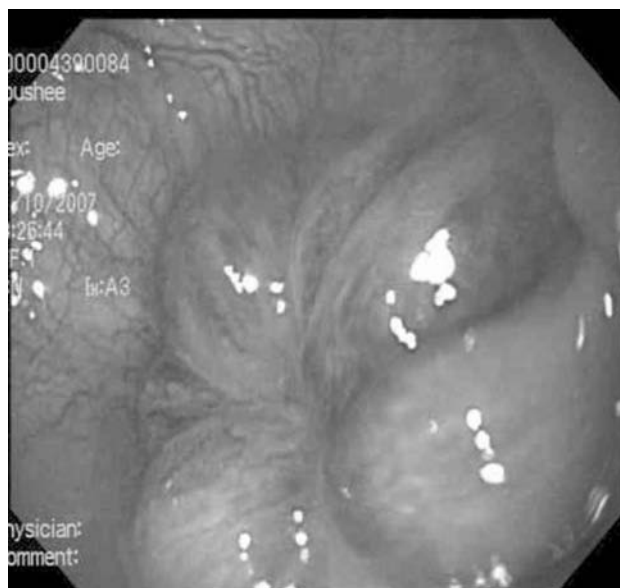
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**Purpose:** Downhill esophageal varices are a rare, but recognized entity usually due to complications from superior vena cava syndrome. We present a case of a 29-year-old healthy female who was referred to our open access endoscopy unit for the chief complaint of chronic intermittent dysphagia. She also complained of odynophagia.

Her past medical and family history were unremarkable and her physical exam normal.

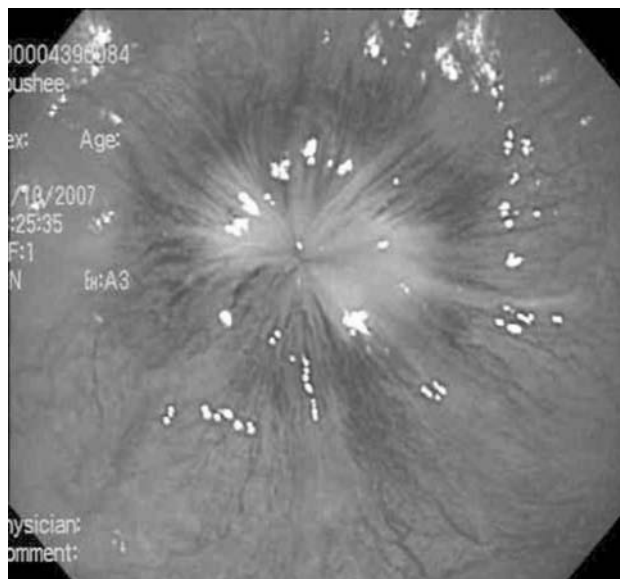
Endoscopy was indicative of a hypertonic lower esophageal sphincter. Blanching of the mucosa and formation of varices were evident during

LES contraction. [figure1] Upon relaxation of the LES, the blanching of the mucosa and the varices were no longer evident. Subsequent evaluation excluded primary liver disease and portal hypertension as possible etiologies. Esophageal manometry showed a hypertensive LES (60 mmHg) with long duration (10–12 secs), high amplitude contractions reaching 302 mmHg in the distal esophagus. However, many of the swallows were peristaltic thereby excluding achalasia.



With a paucity of MEDLINE citing, this presentation may be one of the first reported cases of downhill varices in a healthy individual without a previously well-known anatomical etiology and the result of esophageal dysmotility. The hypertensive LES could very well impede blood flow from the azygous, hemiazygous, short gastrics, the left gastric, and the left inferior phrenic veins and their collaterals leading to the transient formation of varices.

One could also speculate that the patient's odynophagia was the result of decreased blood flow and transient ischemia as evidenced by the pronounced blanching of the mucosa over the area of the LES and distal esophagus during LES contraction. [figure2] Following relaxation the mucosa overlying the LES and lower esophagus regained their normal pink appearance and the varices decompressed.



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### Use of Pillcam ESO™ Endoscopy for Early Detection of Esophageal Injury after Radiofrequency Ablation Therapy for Atrial Fibrillation

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**Purpose:** Atrial-Esophageal fistulas are an increasingly recognized complication of radiofrequency ablation (RFA) therapy for atrial fibrillation. This potentially fatal complication is often undiagnosed until late in its development. The purpose of this study is to evaluate utility of esophageal capsule endoscopy in early identification of RFA related esophageal injury, therefore recognizing patients with need for more intense post-ablation follow-up and treatment.

**Methods:** A retrospective chart review of patients that received esophageal capsule endoscopy post RFA therapy was completed. All patients had been examined using Pillcam ESO™ and the Given Imaging System™ in the manufacturer recommended fashion. The video was reviewed by a board certified gastroenterologist. The first esophageal image, Z-line, first gastric image and any pathology were identified and marked by thumbnail still images. After review of the entire video, each thumbnail image was re-examined and the final results were recorded. Medical records were subsequently reviewed for patient's demographics, and immediate postablation symptoms.

**Results:** A total of 32 patients (72% male, mean age 60 years old) were reviewed for this study. 15 patients (47%) had symptoms after ablation: chest discomfort or pain (9/32, 28%), nausea (6/32, 18%), abdominal pain (1/32, 3%) and fever (1/32; 3%). Three patients had moderate difficulties swallowing the capsule (3/32; 9%), all patients completed the capsule exam. We identified positive findings in 7 patients (7/32; 22%). 4 of these patients did not have any symptoms post ablation. 3 patients with positive findings had symptoms, one each with chest pain, abdominal pain and nausea. In 4 of the patients the lesion was described as linear erosion with clean base in distal esophagus, just above or at Z line (4/32; 12.5%). In 3 of the patients the lesion was described as mid esophageal ulceration (3/32; 9%) with or without trace of blood.

**Conclusion:** Our preliminary data suggest that capsule endoscopy can be a useful tool for early diagnosis of esophageal injury after RFA. More detailed studies are planned to delineate best timing for capsule endoscopy, array of lesion appearances, best strategy to exclude pre-existing lesions and post-capsule endoscopy treatment protocols for patients with positive findings.

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### Atypical GERD Symptoms on PPI Therapy Are More Likely in an Older Female Patient Group

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**Purpose:** Initiating PPI therapy on patients who present with symptoms of GERD has become the diagnostic and therapeutic standard of care. Many patients, however, present with ongoing symptoms, which range from the typical symptoms of heartburn, regurgitation, and chest pain to atypical symptoms such as cough, throat clearing, and hoarseness. Demographic characteristics of patients presenting with typical or atypical symptoms have not been identified.

**Aim:** To determine if gender and age differences are present in patients on PPI therapy who present with typical versus atypical symptoms.

**Methods:** A retrospective analysis of 200 consecutive patients who have undergone MII-pH from January 2005 to October 2006 was performed. All patients had residual symptoms despite twice daily PPI therapy, and were studied on treatment. Questionnaires asking patients to identify the most bothersome symptom were reviewed, as was the age and gender of

each patient. Typical symptoms included heartburn, regurgitation, and chest pain. Atypical symptoms included cough, hoarseness, throat clearing, nausea, wheezing, globus, belching, indigestion, and shortness of breath.

**Results:** The tables below summarize our review.

**Table 1.** Gender analysis

	# Males	# Females
Typical symptoms	42	57
Atypical symptoms	28	73

$P < 0.05$  by chi-square

**Table 2.** Age analysis

	# patients	Mean age
Typical symptoms	99	53
Atypical symptoms	101	57

$P < 0.05$  by t-test

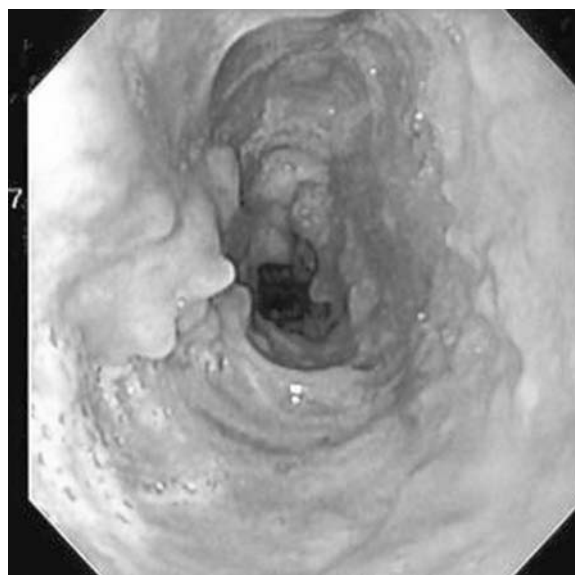
**Conclusion:** Patients presenting with atypical GERD symptoms on PPI therapy are more likely to be female and older than those with persisting typical symptoms.

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### An Unusual Case of Esophageal Histoplasmosis

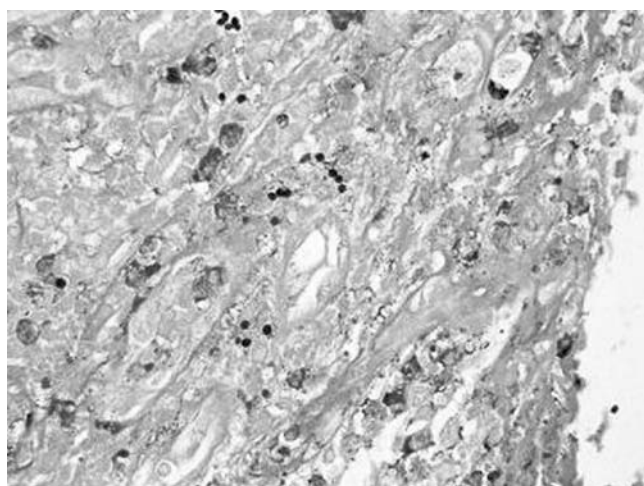
Kanan Sharma, MD, Pallavi K. Rao, MD, Lisa Stone, MD\*. Department of Gastroenterology, Wright State University, Dayton, OH.

**Purpose:** A 44 year-old African American female with HIV, CD4 count of 8, non-compliant on HAART, presented with dysphagia and odynophagia of two months duration. She also had weight loss of 50 lbs over same period. About six months ago, she was treated for PCP, oral candidiasis and meningitis. At presentation, her vitals were stable. She appeared cachectic without any evidence of oral thrush. The laboratory values revealed WBC count of 5400, hemoglobin of 8.3 and albumin of 2.8. Her chest x-ray did not show any abnormalities. She was empirically started on diflucan and acyclovir for possible candida esophagitis and herpes esophagitis, respectively. EGD showed diffuse deep ulcers with irregular borders with friable mucosa and nodularity involving the entire length of esophagus. Esophageal biopsies were positive for histoplasma capsulatum on Gomori's methenamine-silver and periodic acid-Schiff stains. Her blood, urine and sputum cultures were



negative. A urine and serum histoplasma antigen test was negative. She was subsequently started on itraconazole with improvement of dysphagia.

**Discussion:** Histoplasma capsulatum, a dimorphic fungus, is frequently encountered to cause opportunistic infections in immunocompromized hosts. In AIDS patients with disseminated histoplasmosis, symptomatic gastrointestinal tract involvement has been reported in 3–12% of cases. The most commonly reported sites of infection are colon followed by small bowel. Esophageal involvement with histoplasmosis is very rare, almost always occurring either due to mediastinal adenitis or mediastinal fibrosis. Our patient presented with dysphagia leading to the diagnosis of esophageal histoplasmosis without signs of pulmonary or systemic histoplasmosis. The diagnosis of histoplasmosis requires a high index of suspicion, more so in patients living in endemic areas.[figure1][figure2]



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#### Adenosine – A Key Neuromediator in the Pathogenesis of Functional Chest Pain

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**Purpose:** Adenosine lowers sensory thresholds and decreases distensibility of the esophagus suggesting that it may play a role in the pathogenesis of esophageal hypersensitivity (Neurogastro Mot 2006; 18: A713). However, it is not known whether the adenosine induced alterations in esophageal sensorimotor function of healthy humans are akin to those observed in patients with functional (non-cardiac) chest pain (FCP). Our aim was to compare the sensory and biomechanical properties of esophagus in patients with FCP with those of healthy controls during adenosine infusion.

**Methods:** In a randomized, double-blind, placebo-controlled study, 14 healthy subjects (M/F = 4/10), received either adenosine or placebo infusion, IV at 100 µg/kg/min. During infusion, subjects underwent stepwise graded balloon distensions of the esophagus (EBDT) using impedance planimetry. Sensory responses and biomechanical properties were assessed. One hour before infusion, impedance planimetry was performed to assess baseline sensori-motor properties. EBDT was also performed in 14 matched patients with FCP (Rome II). Data were analyzed for 7 controls who received adenosine with 14 FCP patients using ANOVA and paired t test.

**Results:** (Table, mean ± SEM). When compared to controls at baseline, FCP patients had lower thresholds for sensory perception ( $P < 0.05$ ), larger ( $P < 0.05$ ) Cross Sectional Area (CSA) and decreased ( $P < 0.05$ ) esophageal wall strain. Also, in controls, during adenosine infusion, sensory thresholds decreased significantly ( $P < 0.05$ ). The CSA and reactivity of the esophagus increased, whereas wall strain decreased ( $P < 0.05$ ), when compared

to baseline. Sensorimotor properties were similar between controls (after adenosine infusion) and FCP ( $P > 0.05$ ).

**Conclusion:** In healthy controls, the adenosine-induced changes in esophageal sensorimotor function, notably hypersensitivity and decreased distensibility, were identical to those observed in native patients with FCP. Thus, adenosine may be a key mediator in esophageal hyperalgesia and sensorimotor dysfunction of patients with functional chest pain.

Sensory & biomechanical properties	Controls		
	Baseline	Adenosine	FCP
Threshold- first perception (cm H <sub>2</sub> O)	33 ± 7*	12.5 ± 6	14.4 ± 5
Threshold-discomfort (cm H <sub>2</sub> O)	55.5 ± 5*	31 ± 11	38.4 ± 6
Threshold-pain (cm H <sub>2</sub> O)	68.5 ± 8*	52.5 ± 9	51.2 ± 8
CSA at 40 cm H <sub>2</sub> O (mm <sup>2</sup> )	440 ± 54*	520.7 ± 179	558 ± 144
Reactivity at 40 cm H <sub>2</sub> O	145 ± 86	249.2 ± 152	171 ± 86
Strain at 40 cm H <sub>2</sub> O	1.3 ± 0.1*	0.8 ± 0.3	0.9 ± 0.1

\* $P < 0.05$  compared to FCP patients and Adenosine

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#### A PPI Is a PPI! Similar Results for Continuous Reflux on Therapy

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**Purpose:** 24 hour multichannel intraluminal impedance and pH (MII-pH) esophageal monitoring allows detection of both acid (pH < 4) and non-acid (pH > 4) gastroesophageal reflux (GER) episodes. Many GERD patients experience symptoms despite PPI therapy. It was recently proposed that revision of the upper limit of normal for reflux episodes on PPI therapy to 48 should be used to identify patients with abnormal number of reflux episodes while on 24 hours acid suppression therapy (Tutuian et al. Gastroenterology 2006; 130:S1184).

**Aim:** To compare the total number of reflux episodes (both acid and non-acid) in patients treated with bid doses of different PPIs.

**Methods:** 167 consecutive MII-pH studies (109 females; mean age 43 years; range 7.5 months – 85 years) on bid PPI therapy were analyzed. The total number of reflux episodes (both acid and non-acid) during treatment with esomeprazole, omeprazole, lansoprazole, rabeprazole, and pantoprazole were recorded.

**Results:** The table below summarizes the results.

PPI	# patients (%)	Mean # of GER episodes/24 hr (non-acid/acid)	# patients with abnormal GER (%)
Esomeprazole	75 (45%)	35 (27/8)	24 (32%)
Omeprazole	13 (8%)	35 (30/5)	4 (31%)
Lansoprazole	45 (27%)	37 (28/10)	14 (31%)
Rabeprazole	18 (11%)	34 (29/5)	4 (22%)
Pantoprazole	16 (9%)	34 (27/8)	4 (50%)

There was no difference ( $P > 0.05$ ) in the number of GER episodes when comparing different PPI therapy. Using the revised criterion for abnormal reflux episodes/24 hours on PPI bid of 48, there was no difference ( $P > 0.05$ ) in the number of patients with abnormal GER on different PPI therapy. There was a difference ( $P < 0.05$ ) in the number of non-acid and acid reflux

episodes on PPI therapy, with continuing reflux 3–4 times more likely to be non-acid in type.

**Conclusion:** Continuing GER occurs despite PPI therapy, although it is predominantly non-acid in type. Total number of reflux episodes are similar in patients on different PPI therapies.

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### A Novel Partial 5HT<sub>3</sub> Agonist DDP733 after a Standard Refluxogenic Meal Reduces Reflux Events: A Randomized, Double-Blind, Placebo-Controlled Pharmacodynamic Study

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**Purpose:** Transient lower esophageal sphincter (LES) relaxations are the major cause of gastro-esophageal reflux. DDP733, a selective partial agonist at 5HT<sub>3</sub> receptors, increases LES in experimental animal models. However, its effect on gastroesophageal reflux or LESP in humans is unknown.

**Aims:** To evaluate the effect of DDP733 on reflux episodes in healthy volunteers receiving a refluxogenic meal, and to assess the safety and tolerability of DDP 733.

**Methods:** A randomized, double-blind, placebo-controlled crossover study evaluated the pharmacodynamic effects of DDP733. Subjects were randomized on a 1:2:1 basis to one of three dose levels of DDP733 (0.5 mg, 0.8 mg, 1.4 mg), and randomized to the order of administration of placebo or active drug. Healthy subjects underwent manometry, and intraesophageal multi-channel intraluminal impedance and pH after a standard refluxogenic meal. For evaluating the safety and tolerability of DDP733, each subject took drug or placebo (three times daily) for one week. A pooled analysis of variance, of the within subject deltas (placebo-drug) over all three dose groups with dose specific tests ( $\alpha = 0.017$ ) for no change were examined.

**Results:** DDP733 0.5 mg significantly reduced the rate of reflux episodes after refluxogenic meal from 10.4 ( $\pm 2.2$ ) on placebo to 6.3 ( $\pm 1.2$ ) on drug over a 2 hour period. However, DDP733 0.8 mg and 1.4 mg had no significant effect on reducing the number of reflux episodes (table). Significant differences in LESP and the proportion of time pH was  $<4$  (placebo-drug) after a reflexogenic meal were not detected. No serious adverse events on DDP733 were reported.

**Conclusion:** In healthy subjects, the partial 5HT<sub>3</sub> agonist DDP733 at a dose of 0.5 mg significantly reduces the rate of reflux events, but did not result in a significant change in LES pressure at one hour post dosing.

Reflux events, post treatment mean LESP, and proportion time that time pH $<4$ on drug or placebo (Mean $\pm$ SEM)						
	DDP733 0.5 mg		DDP733 0.8 mg		DDP733 1.4 mg	
	Drug (N = 7)	Placebo (N = 7)	Drug (N = 14)	Placebo (N = 14)	Drug (N = 6)	Placebo (N = 5)
Reflux events (n)	6.3 $\pm$ 1.2	10.4 $\pm$ 2.2	8.9 $\pm$ 1.1	6.9 $\pm$ 1.1	9.3 $\pm$ 2.1	12.0 $\pm$ 1.3
	$P = 0.013$		$P = 0.069$		$P = 0.340$	

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### Esophageal Histology in Patients with Gastroesophageal Reflux Disease (GERD) and Symptom Resolution after 4 Weeks of Esomeprazole Treatment

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**Purpose:** To estimate the prevalence of histological findings related to acid exposure in patients with symptoms of GERD, with or without erosive

esophagitis (EE), and to associate heartburn (HB) resolution after 4 weeks of esomeprazole treatment with baseline histology.

**Methods:** This was an exploratory analysis of histology data from a multicenter, open-label study (D9612L00083) in adults (aged 18–70 y) with HB  $\geq 2$  d/wk for the past week and on average during the past 3 months. During a baseline endoscopic examination of the esophagus, 3 biopsy samples each were taken from 1 cm (distal) and 3 cm (proximal) above the gastroesophageal junction. A 1:1 subset of patients with and without EE was admitted into a treatment phase and received esomeprazole 40 mg daily for 4 weeks. Biopsy specimens were processed in a central laboratory and evaluated by a single observer (W.M.W.). The histological diagnosis was classified as none, mild, moderate/severe, or eosinophilic esophagitis based on basal cell thickness), papillary height), neutrophil counts), and eosinophil counts. GERD symptoms were assessed at baseline and week 4, with symptom resolution defined as patients recording none on a scale of none, mild, moderate, or severe.  $\chi^2$  and Cochran-Armitage tests were performed to test for, respectively, differences and trends in proportions.

**Results:** Of 399 patients who underwent endoscopy, 356 were part of the intention-to-treat (ITT) treatment group. Among assessable patients without eosinophilic esophagitis, significantly more EE patients had baseline histological findings related to acid exposure than non-EE patients (proximal, 86% vs 72%, respectively;  $P = .001$ ; distal, 93% vs 84%, respectively;  $P = .013$ ). There was a shift toward greater histological severity in EE versus non-EE patients. In the ITT population, there was a trend toward greater HB resolution rates, with more severe diagnoses in the proximal ( $P = .027$ ) but not the distal ( $P = .48$ ) esophagus.

**Conclusion:** More EE than non-EE patients had histological findings at baseline that were consistent with acid exposure, with a shift toward greater severity in EE vs non-EE patients. After 4 weeks of esomeprazole treatment, patients who had more severe baseline histological changes in the proximal region of the esophagus tended to have greater HB resolution.

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### Barrett's Esophagus and Helicobacter pylori Infection

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**Purpose:** Barrett's esophagus (BE) is generally accepted as a complication of chronic and severe GERD. The relationship between H. pylori (HP) and BE is controversial. Some reports indicated that HP eradication may increase the symptom of GERD, which may lead to increase a risk of developing BE. This study is to show whether there is an increased occurrence of HP in BE by using a multiplex PCR technique.

**Methods:** This study was performed in 28 patients with BE and 104 patients with dyspepsia undergoing endoscopy in Evanston Northwestern Healthcare. The specimens were collected from both distal esophagus and corpus/antrum. H. pylori infection was detected by one-step multiplex PCR method.

**Results:** Of the 28 patients with BE, 86%(24/28) were detected with HP infection; 75%(21/28) at the distal esophagus and 61%(17/28) at the corpus/antrum. Of the 104 patients with dyspepsia, HP infection was found in the 53.85% (56/104); 32.69%(34/104) at the distal esophagus and 44.23%(46/104) at the corpus/antrum.

**Conclusion:** In our study, the prevalence of HP infection in BE is 75%(21/28) at the distal esophagus, in the Barrett's segment with columnar epithelium, which is significantly higher than 32.7%(34/104) at the distal esophagus with squamous epithelium, in cohorts of patients with dyspepsia ( $P < 0.0001$ ). It is different from some previous reports which indicated that HP organisms do not colonize the specialized intestinal metaplasia characteristic of Barrett's esophagus, because of the high sensitivity and specificity of the multiplex PCR. If indeed HP is commonly found in BE, HP might have played a significant role in the pathogenesis of BE in patients with reflux esophagitis. Some researchers believe that when the infection induces corpus-predominant gastritis, there may be concomitant reduced gastric acid

secretion and eradication of the bacteria in this subgroup of patients may enhance gastric acid secretion and provoke reflux symptoms. It is assumed that the increase in reflux symptom leads to increase in number of esophageal cancer. The increase in the occurrence of HP in Barrett's segment may serve as a co-carcinogen, with reflux symptom, leading to dysplasia and/or carcinoma.

Clinical Status	Number of Cases	H. pylori Infection Distribution Detected By MPCr					
		E	G	E or G	E and G	E only	G only
Barrett	28	21	17	24	14	7	3
Dyspepsia	104	34	46	56	22	24	10
Total	132	55	63	80	36	31	13

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### PPI Efficacy in Overweight/Obese Patients with Erosive GERD: Rabeprazole (RAB) 20 mg vs Omeprazole (OME) 20 mg

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**Purpose:** Obesity is increasing worldwide and elevated BMI is associated with erosive esophagitis (EE). Limited data exist on the efficacy of PPIs among overweight/obese patients. This analysis assessed the efficacy of RAB vs OME in normal weight (<25 kg/m<sup>2</sup>) and overweight/obese (≥25 kg/m<sup>2</sup>) subjects.

**Methods:** Post hoc analysis by BMI of a multicenter, double-blind, parallel group, randomized trial of RAB 20 mg or OME 20 mg once daily for 4 to 8 weeks (Pace Dig Liver Dis. 2005). Patients (N = 560) had endoscopic evidence of Savary-Miller grade I-III EE, moderate to very severe reflux symptoms, and heartburn for ≥3 days during each of the 2 wks before enrollment. Patients recorded daily symptom severity. Endoscopy was performed at Wk 4 and Wk 8 if not healed at Wk 4. Treatment efficacy by BMI was analyzed using log-rank and Cochran-Mantel-Haenszel tests.

**Results:** Percentage of EE healing (primary endpoint) did not differ between treatment groups within each BMI category or by BMI category within treatment groups. In the overweight/obese group, statistically significant differences favoring RAB were seen in time to 1st day of satisfactory heartburn relief; % complete heartburn relief in each of the first 3 and 7 days of treatment; and % satisfactory heartburn relief in the first 3 days (all *P* < .05). Numerical trends favoring RAB in both BMI groups were also observed in other secondary endpoints analyzed.

**Conclusion:** EE healing did not differ with RAB 20 mg and OME 20 mg in either BMI group. In overweight/obese patients, RAB may be more effective than OME in heartburn relief in the first week. *Sponsored by Eisai Inc; Ortho-McNeil Janssen Scientific Affairs, LLC; Janssen-Cilag.*

	BMI < 25 kg/m <sup>2</sup>		BMI ≥25 kg/m <sup>2</sup>	
	RAB	OME	RAB	OME
PP Population	90	79	143	158
(1° Endpoint) (n)				
EE healing,	88.9/96.7	89.9/97.5	92.3/98.6	89.9/97.5
4 wks/8 wks (%)				
ITT Population	93	80	152	163
(2° Endpoint) (n)*				

Time (days) to 1st day of satisfactory heartburn relief – mean	3.1	5.0	2.6†	3.8
% satisfactory heartburn relief				
First 3 days	52.7	48.8	59.2†	46.6
First 7 days	46.2	40.0	53.3	42.3
% complete heartburn relief				
First 3 days	35.5†	21.3	38.2‡	23.9
First 7 days	31.2†	17.5	32.9‡	19.6

\*Patients with value for listed variable (N = 542 ITT patients). †*P* < .05 vs OME. ‡*P* < .01 vs OME.

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### Use of Narrow Band Imaging (NBI) To Detect Esophagitis in Non Erosive Reflux Disease (NERD)

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**Purpose:** Most patients with reflux symptoms do not have signs of mucosal injury on routine endoscopy. In patients with non erosive reflux disease (NERD) chromoendoscopy with Lugol's iodine and confocal laser endomicroscopy have been reported to identify lesions with histologic evidence of esophagitis. However, both procedures are time consuming and require the use of contrast agents. Narrow band imaging (NBI) is known to display macroscopic lesions such as ulcers with high contrast and clarity. We report our findings in an initial group of patients with persistent reflux symptoms and a normal esophagus on white light (WL) endoscopy to see if erosive lesions could be detected with high contrast NBI endoscopy.

**Methods:** The Olympus GIF-H180 gastroscope was used in five patients; 3 male, 2 female, with a mean age of 49 (range 22–63) who underwent upper endoscopy for persistent reflux symptoms (heartburn at least 3 times per week for more than 3 months). On finding no evidence of esophagitis on WL endoscopy in all 5 patients, the NBI mode was switched on and the esophagus re-examined. Any discrete lesions were photographed and biopsies taken with cold forceps for histology. If no lesions were seen, biopsies were taken from the distal esophagus.

**Results:** In asymptomatic individuals, NBI displays the normal esophagus with an even blue color. On switching to narrow band imaging (NBI) mucosal breaks or erosions were seen in 4 out of 5 patients (80%). These consisted of: 1) discrete, depressed erosions of up to 1 mm in diameter, surrounded by an even, bluish appearing normal squamous mucosa; 2) larger, flat, depressed, magenta colored patches of up to 10 mm in diameter, with visible raised margins. Targeted biopsies from these lesions showed microscopic evidence of reflux esophagitis in all 4 patients (100%). Biopsies from the distal esophagus of the patient without mucosal lesions were normal.

**Conclusion:** These early findings suggest that high contrast imaging methods such as NBI may be useful in unmasking subtle erosive changes in the esophagus of patients with reflux symptoms that are not readily visible on routine white light endoscopy. High contrast imaging with NBI is a rapid and easy technique that does not require complex instrumentation or dyes. If these initial findings are verified by future studies, this may become a useful technique for identifying erosive lesions and targeting biopsies in patients with presumed NERD.

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### Cervical Inlet Patch in Twins: Is It All in the Genes?

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**Purpose:** Cervical inlet patch (IP) is a distinct region of heterotopic gastric mucosa occurring in the proximal one-third of the esophagus. The

pathogenesis of IP has not yet been finally determined. It is considered to be congenital by some, acquired by some, and considered to be congenital with superimposed acquired component by others. We report the cases of identical twins with identified IP; this lends support to the theory that IP is a congenital rather than an acquired entity.

**Case Report:** Two 41 year old identical male twins presented with retrosternal discomfort a little over one year apart. These symptoms were present in both individuals for several years. Esophagogastroduodenoscopy (EGD) revealed a single inlet patch in one twin and dual inlet patches in the other. In both individuals, IP was seen in the upper esophageal sphincter. There was no evidence of Barrett's esophagus in either. Biopsy revealed oxyntocardiac mucosa with mild chronic inflammation. There was no evidence of intestinal metaplasia. Immunohistochemical stain was negative for *Helicobacter pylori*. Both of them had alleviation of symptoms with treatment using a proton pump inhibitor.

**Discussion:** IP occurs with a prevalence of 0.1% to 10% in patients undergoing EGD. It has been shown to be associated with symptoms like heartburn and dysphagia along with complications such as esophagitis, perforation, and adenocarcinoma. It can also cause supraesophageal symptoms such as cough and hoarseness. However, the origin of inlet patch has been a source of debate. Chatelain *et al.* have demonstrated that IP shares some common features with Barrett's esophagus, and as such they may have a common pathogenesis, related to reflux disease. Autopsy studies have reported an incidence of 4.5% in infants and 11.8% in children, thus suggesting it is congenital. According to a 'mixed theory', there could be a loss of squamous epithelium due to regurgitation or trauma and subsequent surfacing of congenitally present ectopic gastric mucosa. This occurrence of IP in identical twins supports the latter two theories of formation.

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### Risk of Barrett's Esophagus in Patients Who Undergo Bariatric Surgery: A Retrospective Analysis

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**Purpose:** Obesity and gastroesophageal reflux disease (GERD) are associated with Barrett's esophagus (BE) and increased risk of esophageal adenocarcinoma. We evaluate the risk of BE in patients who undergo gastric bypass surgery. Long standing GERD in obese individuals may induce or protect from BE formation due to alkaline reflux or gastroparesis or some unidentifiable factors. The true risk of Barrett's in patients who are obese and undergo Bariatric surgery is not well known. The objective of the study is to evaluate the risk of Barrett's esophagus in patients who undergo Bariatric surgery.

**Methods:** Tertiary care center, inpatient. *Study Design:* Retrospective chart review study. *Inclusion criteria:* All adult patients who underwent bariatric malabsorptive gastric reduction surgery (Roux-en-Y) and esophagogastroduodenoscopy (EGD) for any reason after the surgery were included. *Primary end point:* Patients with endoscopic and histological evidence of BE.

**Results:** We reviewed the charts of 120 patients undergoing gastric bypass surgery between June 2001 and March 2007. Mean age of the study population was 47.1 years with majority of the patients represented by Caucasians (89.2%) and females (86.5%). Thirteen patients among the 120 patients were excluded (8 – insufficient documentation, 4 – EGD prior to surgery, 1 – BE diagnosed on EGD prior to surgery). The most common indications for EGD were nausea and vomiting and abdominal pain. 20 patients of the remaining 107 patients met study criteria (underwent EGD after the surgery). The time between bypass surgery and EGD ranged from 1 to 52 months, with a mean of 17.7 months. BE was not detected in our study group. However, one out of these 20 patients had esophageal adenocarcinoma diagnosed at 15 month follow-up EGD. This patient did not have EGD prior to surgery raising the question of an incidental finding. The most common EGD findings in this population were normal (13) and marginal ulcer (4).

**Conclusion:** Based on our limited retrospective study, the risk of Barrett's esophagus appears to be very low in post-bariatric surgery patients. Further long-term prospective trials should be performed to evaluate the true risk in this subset of population.

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### Value of a Novel Multi-Factorial Scoring System as a Diagnostic Aid in the Prospective Evaluation of Patients with Reflux-Like Dyspepsia

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**Purpose:** Reflux-like dyspepsia (RLD), where predominant epigastric pain is associated with heartburn and/or regurgitation, is quite prevalent and has variable response to proton pump inhibition (PPI) therapy. Since symptom frequency and severity vary, there is frequent overlap among gastroesophageal reflux disease (GERD), non-erosive reflux disease (NERD) and RLD. We assessed the potential of an algorithm and a multi-factorial scoring system in discriminating patients presenting with RLD from those with true GERD or NERD.

**Methods:** We prospectively evaluated an outpatient, community-based, cohort presenting with RLD using the following algorithm: After an initial symptom evaluation (epigastric pain, heartburn, regurgitation, dysphagia), endoscopy and distal esophageal biopsies were performed to evaluate the structure of the esophagus, stomach and duodenum, followed by esophageal motility and 24-hr ambulatory pH monitoring to assess esophageal function and pathologic acid exposure.

**Results:** 110 patients (35 men, 75 women) were evaluated. Endoscopy showed erosive or complicated GERD in 33 patients (30%) and it was normal in 77 patients (70%). Of this latter group, 62 (56%) had abnormal pH and motility studies and were classified as patients with NERD. The remaining 15 (14%) had normal functional studies and were classified as patients with RLD. A disease severity score was then applied (Table). The scoring system effectively distinguished patients with GERD (mean score 8.69, range 5–15), NERD (mean score 6.22, range 3–10) and RLD (mean score 3.27, range 2–4). A score higher than 4 excludes RLD; a score higher than 10 excludes NERD.

**Conclusion:** An algorithmic evaluation and scoring of patients presenting with RLD effectively distinguishes patients with NERD and GERD from those with functional RLD, facilitates long-term management and defines the need for continuous PPI therapy.

#### Components of disease severity score.

Variable	0 points	1 point	2 points	3 points
Epigastric pain	absent	present		
Heartburn	absent	present		
Acid regurgitation	absent	present		
Dysphagia	absent	present		
Endoscopy	Normal	Esophagitis/ ulcer	Stricture	Barrett's esophagus
Hiatal hernia	absent	≤2 cm	>2 cm	
Esophageal biopsy	Negative	Inflammation	Barrett's esophagus	
DeMeester score	≤15	16–25	26–50	≥51
LESP (mmHg)	>10	≤10		

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### Clinical Utility of Impedance in Evaluation of Noncardiac Chest Pain

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**Purpose:** Noncardiac chest pain (NCCP) is a common clinical dilemma. The significance of acid and nonacid reflux in patients with noncardiac chest pain is not fully understood, especially in patients with chest pain refractory to PPI therapy.

**Aim:** To evaluate characteristics of acid and nonacid reflux in a cohort of patients with noncardiac chest pain referred for 24 hour impedance testing.

**Methods:** A retrospective chart review was performed on all 24 hour impedance studies performed at the University of Utah between December 2005 and March 2007. Patient characteristics included age, gender and proton pump inhibitor (PPI) use. Impedance data included acid and non-acid reflux events and symptom associated probabilities (SAP).

**Results:** 24 impedance studies were evaluated. Patient age ranged from 23 to 75 years old. 16 of the 24 patients (67%) experienced abnormal reflux. 13 of these (81%) had nonacid reflux and only 1 had a positive SAP for noncardiac chest pain. 22 of the 24 patients included in this analysis were on a PPI. 16 patients (67%) were women. 11 women experienced poor control of reflux on impedance, 9 of whom had increased amounts of nonacid reflux.

**Conclusion:** The role of acid and nonacid reflux in NCCP is poorly understood. This is the first data set available on the utility of impedance in NCCP. Our data shows that while 92% of the patients were on a PPI, 16 of 24 experienced poor control of reflux symptoms. Of patients with poor control of reflux symptoms, 81% experienced nonacid reflux on impedance. The SAP for patients with both good control and poor control of reflux symptoms does not correlate with the symptom of noncardiac chest pain.

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#### Endoscopic Full-Thickness Plication for the Treatment of GERD: 12 Month Follow-Up in the Sham-Controlled Trial

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**Purpose:** To evaluate the safety and efficacy of the NDO Plicator endoscopic procedure for the treatment of symptomatic GERD in a cohort of patients followed out to 12 months from their original participation in a sham-controlled study.

**Methods:** Patients with chronic heartburn and pathologic reflux requiring daily proton pump inhibitor (PPI) therapy were enrolled. Excluded from treatment were patients with esophageal dysmotility, esophagitis grade III or IV (Savary-Miller), Barrett's epithelium, and hiatus hernia >2 cm. All patients received a single, endoscopically placed full-thickness plication in the anterior gastric cardia. The primary study endpoint was  $\geq 50\%$  improvement in GERD health-related quality of life (HRQL) score. Secondary end points included VAS, SF-36, GERD medication use, and esophageal acid exposure.

**Results:** A total of 148 patients were treated at 14 study sites. No re-treatments were performed. Twelve-months post-plication, 59/96 patients (62%) had improved their GERD-HRQL score by at least 50%. Median percent change in GERD-HRQL score (62%), VAS score (46%), heartburn score (67%) and regurgitation score (50%) were all significantly improved compared to off meds baseline values. The need for daily PPI therapy was either eliminated or reduced by at least half in 63% of patients at 12-months post-treatment. There were no new or late onset adverse events.

**Conclusion:** At 12-months post-procedure, the cohort originally treated with full-thickness plication with the Plicator and the cross-over group treated after sham showed the endoscopic treatment to be safe and effective in reducing GERD symptoms and medication use.

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#### Cryotherapy Ablation for Barrett's Esophagus (BE) with High-Grade Dysplasia (HGD) and Intramucosal Carcinoma (IMCA), and Early Esophageal Cancer (EEC)

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**Purpose:** Endoscopic ablation of HGD/IMCA and EEC is appropriate in selected patients with reasonable life expectancy. The purpose of this study is to assess the safety and efficacy of endoscopy cryotherapy ablation for the elimination of BE with HGD/IMCA and EEC.

**Methods:** This is a single center pilot treatment study of HGD/IMCA and EEC (stage T1/T2 N0 and failed or not amenable to systemic therapy or surgery) using low pressure non-contact liquid nitrogen spray every 4-6 weeks. All patients were assessed with endoscopy/biopsy, endoscopic ultrasound, CT, and PET if cancer was present. For HGD/IMCA: complete response (CR) = absence of BE and dysplasia after 8 treatments; partial response (PR) = BE present with low-grade dysplasia (LGD) or no dysplasia. For EEC: CR = elimination of cancer by biopsy; PR = decrease or stable size of tumor after 8 treatments.

**Results:** 21 patients enrolled (median age 65 years, range 53-93). For HGD/IMCA, 5/16 patients completed treatment with elimination of HGD/IMCA in all 5, persistent BE or LGD in 2, 8 still under treatment. For EEC, 2/5 completed treatment with complete elimination of cancer in 1, stable disease in 1.

Group	Treatment						Removed from study
	N	Complete	CR	PR	Failed	Active	
HGD/IMCA	16	5	3	2	1	8	2
EEC	5	2	1	1	0	2	1
Total	21	7	4	3	1	10	3

No serious adverse events related to treatment occurred. All adverse events were expected and related to treatment. They include chest pain (28%), dysphagia (22%), sore throat (14%), odynophagia (12%), abdominal pain (10%), nausea/vomiting (6%), fever (3%). Patients were removed from the study due to non-compliance (1), severe co-morbid illness (1), or inappropriate enrollment of patient with N1 disease (1).

**Conclusion:** Endoscopic cryotherapy ablation with low pressure liquid nitrogen spray is effective in BE with HGD/IMCA and EEC.

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#### Gender-Related Difference in Composition of Secretion from Esophageal Submucosal Mucous Glands, in Response to Stimulation of Serotonergic Pathway, in Patients with Gastroesophageal Reflux Disease

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**Purpose:** Protective potential of saliva and esophageal secretion in gastroesophageal reflux disease (GERD) patients is well established (Sarosiek J. et al., *J P Gastroenterol* 18: 20J-20Q, 1994). Stimulation of serotonin receptor 5HT-4 with tegaserod augments salivary and esophageal components of pre-epithelial defense in GERD (Majewski et al., *CG&H*, 5:430-8, 2007). The impact of gender on esophageal secretion in GERD patients during stimulation of 5HT-4 receptor remains to be addressed.



**Aim:** To measure the rate of secretion of esophageal protective factors in females (F) and males (M) with chronic heartburn symptoms after 7 days of tegaserod (6 mg BID) or placebo administration.

**Methods:** The study was conducted in 38 GERD patients (26 F & 12 M; mean age of 41) in a double-blind, placebo-controlled, cross-over design. Esophageal secretion was collected during the esophageal mucosal exposure to baseline NaCl, HCl/pepsin and final NaCl, using the esophageal perfusion catheter. Esophageal volume and its content of bicarbonates, non-bicarbonates, mucin, EGF, TGF $\alpha$  and PGE $_2$  were measured using standard methodology.

**Results:** In females after tegaserod, TGF $\alpha$  secretion during the esophageal mucosal exposure to HCl/pepsin solution increased from  $15.0 \pm 2.47$  to  $22.1 \pm 2.71$  pg/min (46.9%,  $P < 0.04$ ). In contrast, in males, TGF $\alpha$  decreased by 51.5%,  $P < 0.03$ . The rate of esophageal EGF secretion in females during administration of tegaserod increased by 145% ( $P < 0.01$ ) whereas in males increased by 50% ( $P > 0.10$ ). The rate of esophageal PGE $_2$  secretion during administration tegaserod increased by 81% ( $P = 0.076$ ) in females only. Males responded by an evident increase of non-bicarbonates (by 69%) during administration of tegaserod, from  $5.29 \pm 0.56$  to  $8.95 \pm 1.89$   $\mu$ Eq/min ( $P = 0.08$ ) and increase of bicarbonates by 143% but not females.

**Conclusion:** 1. A significant enhancement of esophageal protective factors after tegaserod in both genders indicates that secretion of esophageal glands in GERD patients is mediated by serotonergic pathway. 2. The gender-related differences in the serotonergic secretory profiles suggest that 5HT-4 receptors in esophageal glands are influenced by sex hormones.

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### Barrett's Esophagus Surveillance in a VA Population: A 2-Year Retrospective Analysis

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**Purpose:** Barrett's esophagus (BE) has been established as the premalignant precursor to esophageal adenocarcinoma. The aim of this study was to determine the current practice and pattern of surveillance in patients diagnosed with BE in a VA population and to compare them to the current ACG guidelines.

**Methods:** The Denver VA endoscopic database was searched for all patients with a finding of "Barrett's esophagus" on EGD between October 2003 and October 2005. The VA medical record of all identified patients was then reviewed to determine demographic data, EGD findings, pathology results and PPI use.

**Results:** 262 patients (7 F, 255 M; mean age 60 years) had suspected BE including 191 (73%) with biopsy-confirmed BE. Mean length of BE was 3.6 cm (3.4 cm for BE without dysplasia, 4.3 cm for BE with dysplasia). Sixty-four patients had a new diagnosis of BE without dysplasia during the study period of which 9 were excluded due to transfer of care or death. Of the remaining 55 patients, 25 (45%) underwent a repeat EGD with biopsy within a mean time of 15.8 months. Forty-two patients (76%) did not have a repeat EGD with biopsy within 12 + 1 months. The recommendation of the endoscopist regarding timing of follow-up examination ranged from 6 weeks to 5 years in this population. Twenty-five patients (10%) had a new diagnosis of indefinite or low-grade dysplasia during the study period. Four patients were excluded due to transfer of care or death, and 2 additional patients were excluded due to refusal of repeat EGD. Of the remaining 19 patients, 16 (84%) underwent repeat EGD with biopsy within a mean time of 5.1 months. Two patients (11%) did not have a repeat EGD with biopsy within 12 + 1 months. Endoscopist recommendations regarding timing of follow-up examination ranged from 2 weeks to 1 year in this population. One patient had a new diagnosis of high-grade dysplasia on initial EGD with adenocarcinoma found on esophagectomy. Nine patients were diagnosed with esophageal adenocarcinoma on initial EGD. 87% of patients with biopsy-confirmed BE were on PPI therapy.

**Conclusion:** 1) The majority of patients (76%) with BE without dysplasia did not undergo a repeat EGD within 1 year of diagnosis whereas the majority of patients with dysplasia did receive appropriate follow-up. 2) Recommendations regarding appropriate surveillance of BE at our institution are variable among endoscopists. 3) Education regarding practice guidelines may enhance appropriate surveillance of patients with BE.

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### Associated Risk Factors for GERD in Native Americans

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**Purpose:** It is estimated that 30–40% of the US adult population experience reflux monthly and 7–10% report daily reflux. Native Americans (NA) have increased rates of diabetes and obesity which may predispose to reflux. The aim of this investigation is to examine the rates of reflux symptoms and associated risk factors in NAs.

**Methods:** Identical surveys were self-administered to 504 NAs presenting to a primary care clinic at an Indian Health Services facility and 399 non-NA veterans presenting to a primary care clinic at a VA medical center between October 2006 and May 2007. Subjects were queried about the presence and frequency of reflux symptoms. They were also asked demographic and health information including; age, sex and race; height and weight; presence of diabetes, smoking, coronary artery disease, alcohol intake, use of NSAIDS, and consumption of fast food. Chi square analyses were used for proportional data and student t tests were used for means.

**Results:** One hundred eighty-one of 504 (35.9%) in the NA group had reflux symptoms on at least a monthly basis compared with 137 of 399 in the veteran group (34.3%). Group comparisons of demographic data are shown in table one. Results of Chi square analyses for reflux risk factors are shown in table 2. Multiple logistic regression was performed to identify variables that were risk factors for the presence of reflux symptoms. Of evaluated risk factors, CAD (OR 2.01), NSAID use (OR 1.87), smoking (OR 1.79) and fast food consumption (OR 1.96) were identified as independent risk factors for the presence of reflux symptoms. Further, when race was considered, being NA was an independent risk factor for the presence of reflux symptoms (OR 2.37).

**Conclusion:** Being Native American appears to be an independent risk factor for the presence of reflux symptoms with an OR of 2.37. Other identified risk factors included CAD, NSAID use, smoking, and fast food consumption. Obesity and diabetes were not found to be associated with GERD in NAs.

**Table 1.** Demographic information

	Native Americans	Veterans
Mean Age* ( $P < 0.01$ )	46.8	59.0
Percent Men** ( $P < 0.01$ )	34.5	94.2
BMI* ( $P < 0.01$ )	33.3	27.9

\* T-test, \*\* Chi square

**Table 2.** Reflux Risk Factors

	Native Americans	Veterans
CAD ( $P = 0.01$ )	8.4	16.0
ETOH use ( $P < 0.01$ )	19.2	38.6
NSAID use ( $P = 0.04$ )	48.5	38.6
Smoking ( $P < 0.01$ )	12.7	43.4
Fast Food ( $P < 0.01$ )	77.8	59.6

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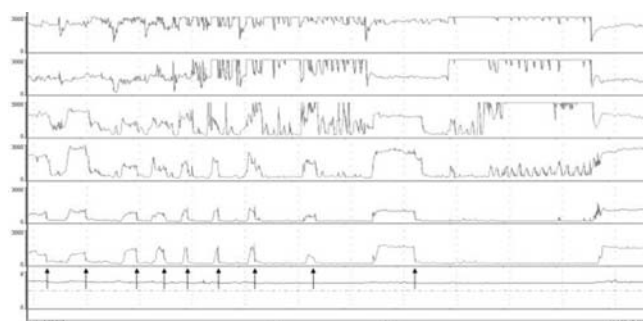
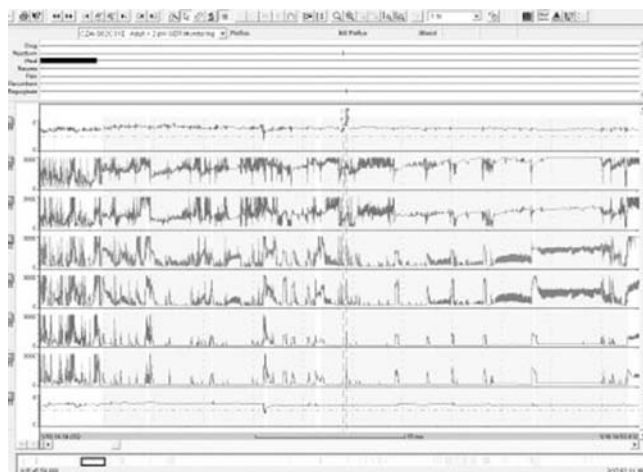
### Esophageal Impedance Detection of Cycling, a Specific Finding in GERD

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**Purpose:** Cycling is a manometric finding specific for GERD, in which repetitive bursts of reflux events are followed by clearance swallows. 24-hr esophageal pH-multichannel intraluminal impedance (MII) can detect this phenomenon in patients with reflux diatheses.

**Methods:** The MII characteristics of cycling identified in 3 patients are described.

**Results:** During routine interpretation of pH-MII studies in our lab, we found 3 patients (all females; 2 with prior bariatric surgery) with post-prandial cycling. All had positive pH-MII studies for nonacid GERD. Their tracings revealed a total of 9 distinct cycling episodes (CycEps) (range 1–5/pt), lasting between 12 and 99 mins (mean 41 min). 7 of 9 CycEps were completely nonacid. The other 2 were predominantly nonacid with very brief acid exposure. At low resolution (30+ min/screen), CycEps had low distal impedance (200–500 ohms) with brief impedance “spikes” that did not reach gas reflux values (Fig. 1). At high resolution, the first GER event in a CycEp was identified by retrograde decreases in impedance to less than 50% of baseline (800–4000 ohms) within the 2 distal channels. Temporary bolus clearance (BC) within a CycEp was identified by sharp antegrade increases in impedance. Subsequent GER events within a CycEp were identified by sharp retrograde decreases in impedance. Because GER events often occurred within seconds of BC, standard MII criteria for BC and GER were not always fulfilled, as impedance between BC and the subsequent GER event did not have time to stabilize (Fig. 2).



**Conclusion:** Cycling can be found on pH-MII studies more frequently than previously recognized, and is a specific marker of persistent GERD. Accurate identification of a CycEp requires manual review of pH-MII tracings.[figure1][figure2]

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### Cost-Effectiveness of MII-pH Testing in Persistent Reflux-Related Cough Despite Acid Suppressive Therapy

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**Purpose:** GERD is a common cause of chronic cough. An empiric trial of high-dose proton pump inhibitor (PPI) is emerging as a diagnostic and therapeutic approach for suspected reflux-related chronic cough. In patients with persistent cough despite adequate acid suppression, symptoms may be due to non-acid reflux or may not be related to reflux. Combined multi-channel intraluminal impedance and pH (MII-pH) detects nonacid reflux and its temporal association with cough. A recent study showed that fundoplication successfully treats non-acid reflux associated cough diagnosed by MII-pH. Cost-effectiveness of this test to aid management of reflux-related persistent cough on PPI therapy has not been studied.

**Methods:** A decision tree was used to compare MII-pH testing to no testing. Cost-utility analysis was performed over a 3 yr time horizon. The published algorithm for management of patients with reflux-related cough refractory to acid suppression defined the care process. The analysis models a hypothetical population of 100 patients with reflux-related cough on acid suppression. We assumed two scenarios: MII-pH testing versus no testing. Costs and quality-adjusted life-years (QALYs) for the two scenarios were examined. Outcome probabilities for the testing arm were derived from published literature (test positive 26%, probability of surgery in test positive arm is 53%). We assumed that cough persisted in all patients in the no testing arm and those patients in the testing arm who did not have fundoplication. The expected costs for this group include PPI use and frequent physician visits. Utilities for persistent cough and no cough health states were obtained from the published literature. Estimated costs of surgery and office visits were obtained from a variety of resources. Drug costs represented the average wholesale price. The primary outcome measured was incremental cost-effectiveness ratio (ICER).

**Results:** MII-pH testing produced an ICER of \$915 per QALY saved compared with no testing, over a 3 yr time horizon. The results are sensitive to the probability of surgery in test positive arm. If we assume that all the patients who are test positive would undergo surgery, the ICER would be \$ 208,671.

**Conclusion:** MII-pH testing to evaluate persistent reflux-related cough refractory to acid suppression cost effectively identifies patients who would benefit from fundoplication.

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### Utility of Endoscopic Ultrasound Prior to Esophagectomy for High Grade Dysplasia in Barrett's Esophagus

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**Purpose:** Esophagectomy is currently recommended as a treatment for HGD. Occult and coexistent cancer (described in up to 50% of patients with HGD undergoing esophagectomy) is a major rationale for esophagectomy. Endoscopic ultrasound is advocated as a method of detecting occult cancers in HGD. We aimed to assess the utility of EUS in detecting cancer in patients undergoing esophagectomy.

**Methods:** We performed a retrospective cohort study of all patients who underwent esophagectomy for HGD at Mayo Clinic, Rochester, from 1994–2005. All patients underwent preoperative endoscopy with biopsies. Patients with carcinoma on preoperative biopsies were excluded. Histology was confirmed by 2 gastrointestinal pathologists. Endoscopic ultrasound (EUS) was performed using radial and linear echoendoscopes by experienced endosonographers. Endoscopic mucosal resection (EMR) was performed using standard techniques. Esophagectomy was performed by experienced thoracic surgeons by the transthoracic or the transhiatal route. Demographic, clinical and pathology data was extracted by review of medical records. Standard statistical tests were used to compare continuous and categorical variables.

**Results:** 70 patients underwent esophagectomy (mean age 60 years [SD10.5]; 67[94%] males) for HGD. The median BE length was 7.5 cm (IQR 5–10.5). 47 patients (67%) underwent EUS and 11 (15%) underwent EMR preoperatively. EMR was done to target visible lesions. Adenocarcinoma was detected on surgical pathology in 9 patients (12.8%). 4 patients had intramucosal carcinoma and 5 had submucosal cancer. None of the patients had metastatic lymphadenopathy. EUS had been performed in 7 of 9 patients preoperatively without detection of occult carcinoma. The prevalence of occult carcinoma in patients who underwent EUS (15%) was statistically similar to the prevalence of occult carcinoma in patients who did not have preoperative EUS (9%) [chi square test 0.44,  $P = 0.50$ ]. There was no esophageal cancer related mortality in this cohort after a mean follow up of 61 months (SD 5.8).

**Conclusion:** Preoperative EUS appears of low utility in the detection of occult carcinoma in patients undergoing esophagectomy for HGD in BE. This is probably due to the early stage of most occult cancers detected at esophagectomy.

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### Refractory ENT/GERD Symptoms – is Upper Esophageal Sphincter (UES) or Esophageal Body the Culprit?

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**Purpose:** Patients with ENT symptoms suspected due to GERD refractory to antireflux therapy present a diagnostic challenge. Significant proportions of these patients have reflux controlled on medication but with little or no symptom relief. Little attention has been paid to potential motility abnormalities – particularly in the UES – in this group.

**Aim:** To review esophageal function studies in patients with ENT symptoms referred for evaluation of refractory GERD.

**Methods:** Retrospective review of esophageal function studies between 07/2003–11/2006. All patients referred by a single ENT specialist were included and esophageal function studies reviewed for presence or absence of abnormalities in the lower esophageal sphincter (LES), esophageal body, and UES. Bolus transit was assessed by simultaneous impedance performed with manometry.

**Results:** Ninety-four of 117 patients referred by this single specialist had esophageal function studies available for review. Symptoms included voice change (45%), chronic cough or throat clearing (30%), heartburn (20%) as well as a variety of other ENT symptoms. Hypertensive UES seen in 29/94 (31%). High residual pressure in 20/94 (21%). UES relaxation duration abnormal in 19 of 94 (20%). Ten of 94 (9%) had hypertensive UES and elevated residual pressure. Overall, 53% had some abnormality in the UES. Ineffective esophageal body motility was seen in 16/94 (17%), otherwise no esophageal body abnormality was consistently seen. Normal viscous and liquid transit was found in 65/94 patients (69%). 29/94 patients had an abnormal transit and in half of these it was limited to either one or the other. LES abnormalities were likewise infrequent in this population.

UES abnormalities are a common finding in ENT patients with symptoms suspected due to GERD refractory to high-dose antisecretory therapy. Motility abnormalities are seen rarely though abnormal bolus transit is seen in a potentially important number of patients.

**Conclusion:** Further studies need to be done to determine if these associations are clinically important.

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### Factors Predictive of a Poor Outcome in Patients with Esophageal Atresia

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**Purpose:** Despite a major improvement in the survival rate of patients with esophageal atresia and tracheoesophageal fistula (EA-TEF), the morbidity associated with this condition remains high. Given this, the aim of our study was to identify early predictive factors of serious complications during the 1st year of life (short term) and after 1 year of age (long term) in these patients.

**Methods:** We retrospectively reviewed the charts of all EA-TEF children born between January 1990 and May 2005. Included cases had been followed at Hopital Sainte-Justine for a minimum of one year. Variables analyzed included different patient characteristics, details of the surgery and early post-operative period. A complicated evolution was defined as the occurrence of at least one of severe gastroesophageal reflux, esophageal stricture needing dilatation, recurrent fistula needing surgery, need for gavage feeding for  $\geq 3$  months, esophageal foreign body impaction needing endoscopic removal, severe tracheomalacia, chronic respiratory disease and death.

**Results:** 152 EA-TEF patients fulfilled our inclusion criteria. 47% were female. Mean gestational age was 36.8 weeks (24–42 wks) and mean birth weight was 2515 g (555–4334 g). 47% had a complicated evolution before one year of age and 45% after one year. Multiple logistic regression demonstrated in the first year of life, 4 groups of significant variables ( $P \leq 0.05$ ) associated with a complex evolution: **Surgery associated issues** (long gap, 2 step surgery, Foker, initial gastrostomy, anastomotic leak) [OR 5.4; 95% CI 1.7–17], **Post-op respiratory complications** (pneumothorax, intubation  $\geq 5$  days p-op, chylothorax) [OR 4.4; 95% CI 1.6–12], **Post-op feeding difficulties** (Inability to feed orally, need for gavage feeding or gastrostomy) [OR 2.6; 95% CI 1.1–6.1], **“other” malformation** not related to VACTERL [OR 2.2; 95% CI 1.0–5.0]. After one year of age, only the **surgery associated issues** [OR 2.8; 95% CI 1.4–5.9] and a **complicated evolution in the first year of life** were predictive of a continued complicated evolution [OR 3.6; 95% CI 1.4–9.2].

**Conclusion:** In children with EA-TEF, we found a number of variables predictive of a high risk of morbidity during the first year of life. Using these variables to identify EA-TEF children at higher risk of complications will allow us to modify their medical management and hopefully reduce their long term morbidity.

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### Eotaxin-3 Immunofluorescence in Adults with Dysphagia: Is There More to Eosinophilic Esophagitis Than Meets the Microscopic Eye?

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**Purpose:** Eosinophilic esophagitis (EoE) is an increasingly recognized chronic, inflammatory disorder characterized by dysphagia and eosinophilic infiltration of the esophageal mucosa. While the pathogenesis remains poorly understood, recruitment of eosinophils is believed to occur in response to allergens and epithelially-derived eotaxin-3. The current diagnosis relies on histologic ( $>20$  eos/hpf) and endoscopic (rings and furrows) findings. Recent studies have shown that H&E staining significantly underestimates both the number of eosinophils and degree of eosinophil degranulation when compared to more sensitive immunohistochemical staining.

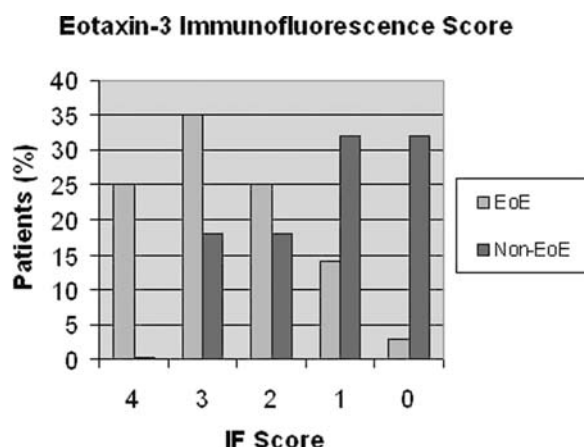
**Aims:** To further define the histologic criteria for diagnosing EoE using eotaxin-3 immunofluorescence in adults presenting with dysphagia.

**Methods:** A total of 51 patients presenting with dysphagia were subdivided based on H&E staining: EoE, GERD, and normal histology. Immunohistochemical staining for eotaxin-3 was performed on all esophageal biopsies.

Immunofluorescence (IF) was assessed by a pathologist who was blinded to the clinical diagnosis and scored on a 0 to 4 scale (0 = no staining to 4 = greatest staining).

**Results:** Of the 51 patients, 29 had a histologic diagnosis of EoE, 13 had GERD, and 9 were normal. The distribution of IF scores are shown in Table 1. The median eotaxin-3 IF score was greater in patients with EoE compared to those with GERD ( $P = 0.008$ ) or normal histology ( $P = 0.006$ ). There was no difference in eotaxin-3 IF scores between patients with GERD vs. normal histology ( $P = NS$ ).

**Conclusion:** Eotaxin-3 immunofluorescence scores were significantly greater in patients with a histologic diagnosis of EoE compared to non-EoE patients. This finding supports eotaxin-3 as an important marker and pathogenic factor for EoE. Esophageal biopsies with eotaxin-3 IF may improve the diagnosis of EoE in patients who present with esophageal symptoms. Patients with refractory GERD and higher eotaxin-3 IF scores may warrant a trial of inhaled corticosteroids.[figure1]



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#### What Is the Incidence of Acidic and Nonacidic Gastroesophageal Reflux (GER) in Lung Transplant Recipients (LTR)?

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**Purpose:** Bronchiolitis obliterans syndrome (BOS) is the most significant cause of mortality in LTR. GER may be a contributing factor in BOS. We evaluated our LTR population to determine the prevalence of acid and nonacid GER and to determine if there is an association between GER, bronchiolitis obliterans syndrome (BOS), and the known BOS risk factor of acute rejection.

**Methods:** Given concerns that GER may cause airway damage after transplant, all living recipients who underwent lung transplant at our institution have been offered pH analysis. These studies were performed off medication and with either standard pHmetry (Sandhill Scientific, Highlands Ranch, CO), or more recently, with impedance technology (Sandhill Scientific, Highlands Ranch, CO). Studies were performed using standard techniques. Each patient's medical record was then reviewed to collect demographic data, confirmed episodes of acute rejection, and pulmonary function data. Patients with prior antireflux surgery were excluded from data analysis. The data were analyzed using SAS software (Cary, NC).

**Results:** To date, 40 patients have had pH studies, and 37 met study criteria. Median age = 41 yrs, 49% were male, and 70% ( $N = 26$ ) had a primary diagnosis of cystic fibrosis (CF). Nineteen of the 37 (51%) had an abnormal pH study (% time with  $pH < 4$  of  $> 4.2\%$ ). Acid exposure in the CF subgroup was significantly increased compared to the rest of the study population. Among CF patients, 16 of the 26 (62%) had an abnormal pH study. There was no significant association between acid reflux and acute rejection or BOS ( $N = 37$ ). However, the CF subgroup ( $N = 26$ ) showed that elevated

acid exposures were significantly associated with a history of acute rejection ( $P = 0.0315$ ). The association between BOS and GER in the CF subgroup also trended toward significance ( $P = 0.192$ ). Fifteen of the 37 patients completed an impedance study. The median total reflux was 40 events and 2/15 patients had significantly abnormal total reflux ( $\geq 73$  events). One of these 2 patients had normal acid exposures.

**Conclusion:** GER is highly prevalent among recipients of lung transplant. In CF patients, there was an association between GER and acute rejection. GER may be injurious to the transplanted lung secondary to reduced pulmonary mucociliary clearance, a diminished cough reflex, and immunosuppressive therapy, thus predisposing to chronic graft rejection.

## STOMACH

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#### The Effect of Tegaserod on Gastric Accommodation and Gastric Emptying in Patients with Functional Dyspepsia and Comparison with Domperidone

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**Purpose:** To investigate The effect of **Tegaserod** on *Gastric Accommodation* and on *Gastric Emptying* in patients with **Functional Dyspepsia** and comparison with **Domperidone**.

**Methods:** 20 patients with functional dyspepsia and 11 normal controls were studied. Using ultrasound, **Gastric Accommodation** was determined by: Fasting water load, Fasting gastric volume, Post drinking gastric volume, Post drinking gastric volume change and The ratio of post drinking gastric volume to fasting gastric volume. **Gastric Emptying** rate was determined by the formula: post drinking gastric volume/post drinking gastric volume after 25 minutes/post drinking gastric volume  $\times 100$ . Then these patients were allocated in two groups: **Group I** included 10 patients put on **Tegaserod** 6 mg twice daily for six weeks. And **group II** included 10 patients put on **Domperidone** 10 mg twice daily for the same period then the previous parameters were re-measured.

**Results:** 1. Post drinking gastric volume change and the ratio of post drinking gastric volume to fasting gastric volume were significantly reduced in patients with functional dyspepsia compared to normal controls:  $802 \pm 322$  and  $585 \pm 242$  ( $P < 0.05$ ) and  $32.9 \pm 16.8$  and  $19.7 \pm 7.2$  ( $P < 0.01$ ) respectively. 2. Gastric emptying rate was significantly reduced in these patients compared to normal controls:  $68 \pm 13.8\%$  and  $44.9 \pm 16.5\%$  ( $P < 0.01$ ) 3. **Group I.** Tegaserod had significant improvement on the ratio of post drinking gastric volume to fasting gastric volume:  $18.7 \pm 7.3$  and  $24.62 \pm 7.88$   $P = 0.02$ . Post drinking gastric volume change was not significantly increased:  $598.7 \pm 222$  and  $635.6 \pm 141.8$   $P = NS$ . The gastric emptying rate was significantly increased in this Tegaserod treated group:  $43.2 \pm 16.7$  and  $54.2 \pm 5.89$   $P = 0.02$ . 4. **Group II.** Domperidone had significant effect on the Post drinking gastric volume change:  $573 \pm 272$  and  $743.5 \pm 71.35$   $P = 0.02$ . The ratio of post drinking gastric volume to fasting gastric volume was not significantly increased:  $20.5 \pm 6.7$  and  $27.1 \pm 11.4$   $P = NS$ . The gastric emptying rate was also not significantly changed:  $46.7 \pm 17$  and  $54.5 \pm 8.89$   $P = NS$ . 5. The improvement in symptoms was reported in 7/10 in the Tegaserod treated group and in 5/10 in the Domperidone treated group.

**Conclusion:** **Tegaserod** was associated with a significant improvement in Gastric Accommodation as well as in Gastric Emptying. **Domperidone** treatment was associated with a significant improvement of Gastric Accommodation but not in Gastric Emptying rate. The improvement of symptoms was more in favour of Tegaserod.

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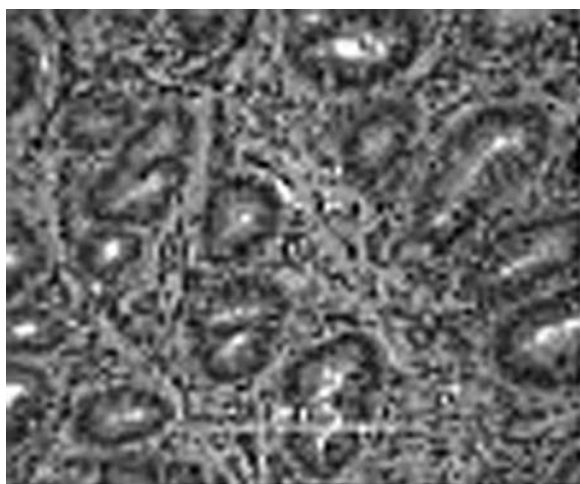
#### Eosinophilic Gastritis: A Case Report

Sumit Sharma, MD, Preeti Agrawal, MD, Jack Garon, MD, Arun Verma, MD\*. Department of Medicine and Department of Pathology, Mt. Sinai Hospital, Sinai Health System, Chicago, IL.

**Purpose:** Eosinophilic gastritis is a rare disorder of unknown etiology and should be suspected in patients when they have unremitting gastric discomfort and routine examination and diagnostics are not able to give a reasonable explanation. It is characterized by patchy/diffuse infiltration of eosinophils in the abdominal wall with peripheral eosinophilia.

**Methods:** A 31 year old Hispanic female with no significant past medical history was referred to the GI service with complaints of chronic vomiting since three years. Vomiting was usually before eating accompanied by mild tenderness in the RUQ. Patient had an EGD done at Mexico in the past, which showed hiatal hernia and esophagitis. There was no history of diarrhea, tenesmus or weight loss. Two days prior to this, patient had abdominal pain with nausea and vomiting for which lansoprazole was prescribed by her primary care physician. The vomiting persisted and abdominal examination showed a soft, mildly tender abdomen with no rebound/signs of peritonitis. Labs showed WBC count of 15,000 with 45% neutrophils, 27% lymphocytes, 5% monocytes and 23% eosinophils. The GI service did an EGD with multiple biopsies to rule out eosinophilic gastroenteritis. The EGD showed moderate sized hiatal hernia, a polyp in the gastric antrum and erythematous mucosa with some nodularity. The GE junction was also irregular with some evidence of nodularity. Biopsy revealed gastric mucosa with marked eosinophilic infiltrates involving the squamous mucosa (Fig. 1: Striking eosinophilic infiltrates, mostly in lamina propria). After ruling out infectious, malignant and other autoimmune causes the patient was diagnosed with Eosinophilic gastritis. She was treated with a low dose of prednisone for a period of four weeks and showed an excellent clinical and biochemical response.

**Results:** We illustrate a case of Eosinophilic gastritis that presented in a way where the diagnosis could have been easily missed. Biopsy in these cases should be taken from both the normal and abnormal appearing mucosa since normal mucosa can harbor diagnostic microscopic appearance.[figure1]



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#### Risk Factors Involved in Patients with Bleeding Peptic Ulcers – A Community Based Study

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**Purpose:** The aim of our study was to 1. Identify the specific risk factors involved in patients with peptic ulcer disease (PUD) and to determine if they predict bleeding in these patients. 2. Determine the frequency of association between non-steroidal anti-inflammatory drug (NSAID) use and *Helicobacter pylori* (*H. pylori*) infection in patients with PUD. 3. Determine if both

rapid urease test and biopsy are necessary to test for *H. pylori* infection in patients with PUD.

**Methods:** We conducted a community-based retrospective case control study. Data analysis occurred using a chi-square test of general association and logistic regression analysis. A total of 230 patients were included in the study between Jan 2004–June 2005 (128 PUD patients with evidence of bleeding served as cases, with a control group of 102 non-bleeding ulcer patients). *H. pylori* infection was assessed by using either rapid urease test or biopsy obtained from the gastric antrum, or both (in 81.7% of patients).

**Results:** There were no statistically significant differences between the bleeding ulcer and control patient groups with respect to gender, age or location of ulcer. However, there was a significantly higher rate of NSAID use in the bleeding ulcer patient group (68.8% vs. 47.6%,  $P < 0.001$ ; unadjusted odds ratio (OR) = 2.42; 95% CI = 1.42–4.51). The rate of *H. pylori* infection was lower in patients with bleeding ulcers (26.6% vs. 39.8%,  $P < 0.05$ ; unadjusted OR = 0.58; 95% CI = 0.31–0.95). There was no interaction between NSAID use and *H. pylori* infection in predicting bleeding ulcer risk ( $P = .08$ ). Sensitivity and specificity for urease test in detecting *H. pylori* was 75% and 99.7%, respectively, with a high positive predictive value of 93.8%. For patients with bleeding ulcers, the sensitivity of urease test was 53.8% versus 80.9% in controls, while specificity was 100% in the case group.

**Conclusion:** NSAID's are associated with an increased risk of bleeding in PUD patients, although the rate of *H. pylori* infection was lower in patients with bleeding ulcers. Our study showed no significant association between these variables. In patients with a positive urease test, biopsy is not needed to confirm *H. pylori* infection which is cost-effective and treatment should be initiated for *H. pylori*. However, due to a high false negative rate, patients with negative urease test results should have biopsy done to confirm evidence of *H. pylori* infection.

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#### One-Day Triple Therapy, Including Immediate-Release Omeprazole, for Eradication of *Helicobacter pylori* Infection

Matthew D. Gaeta, MD, Todd Kilgore, MD, Jeffrey O. Phillips, PharmD, Jack Bragg, DO, John B. Marshall, MD\*. Department of Internal Medicine, University of Missouri Hospital and Clinics, Columbia, MO.

**Purpose:** Regimens to treat *H. pylori* (HP) are cumbersome for patients to take, expensive & frequently associated with undesirable side effects, all of which can negatively affect compliance & eradication rate. To achieve >80% eradication rate requires administration of 3–4 different meds, given for 7–14 days. A recent study found that a 1-day treatment (Tx) regimen of 4 drugs (lansoprazole, bismuth, metronidazole & amoxicillin) gave an eradication rate of 95% (Arch Intern Med 2003;163:2079). Effective 1-day Tx regimens, if confirmed to be effective, would simplify Tx and have great potential to improve patient compliance. An immediate release form of omeprazole (omeprazole/Na bicarbonate; Zegerid) has recently come onto the market. We hypothesized that this agent, which is immediately released, rapidly absorbed into the bloodstream & achieves prompt gastric pH buffering, might hold a clinical benefit over other PPIs when used in 1-day HP Tx regimens.

**Methods:** We conducted a prospective single-arm open-label pilot trial looking at the efficacy of a 1-day regimen of immediate-release omeprazole, in combination with amoxicillin & clarithromycin, to eradicate HP. Patients were eligible for the study if they had HP infection documented by gastric Bx's taken at EGD for dyspepsia. Exclusion criteria included previous Tx of HP, antibiotic Tx in the previous 6 wks, age <18 yrs, pregnancy, allergy to study meds, previous gastric surgery, hepatic insufficiency, IBD, & inability to give informed consent. Of 14 patients with Bx-documented HP infection, 6 met entry criteria and agreed to participate. They received 1-day of therapy with immediate-release omeprazole 40 mg, amoxicillin 1000 mg and clarithromycin 500 mg, with each given for a total of 3 doses (at 0 hrs, 4 hrs & 12 hrs). Patients did not receive any other PPIs during the subsequent study period. Four wks after their Tx, patients underwent urea breath testing

to evaluate for HP eradication. Persistent HP infection was treated with a 14-day triple drug regimen.

**Results:** We found that our 1-day Tx regimen failed to eradicate HP in all 6 patients.

**Conclusion:** This pilot study showed that our 1-day triple drug regimen, which included immediate-release omeprazole, was not effective in the Tx of HP infection. Adding a fourth drug to the regimen could improve efficacy. Further studies of 1-day HP regimens are needed before they can be recommended for routine clinical practice.

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### Report Card To Grade *Helicobacter pylori* Therapies

David Y. Graham, MD\*, Hong Lu, MD, Yoshio Yamaoka, MD. *Medicine, Micheal E. DeBakey VAMC, Houston, TX; Medicine, Baylor College of Medicine, Houston, TX and Digestive Disease, Shanghai Institute of Digestive Disease, Shanghai, China.*

**Purpose:** *H. pylori* causes a serious bacterial infectious disease and the expectations of therapy should reflect this fact. Increasing antibiotic resistance, especially to clarithromycin, has significantly undermined the effectiveness of legacy triple therapy consisting of a proton pump inhibitor, clarithromycin and amoxicillin.

**Methods:** We reviewed current cure rates regarding their ability to achieve an 80% intention-to-treat cure rates, the accepted threshold separating acceptable from unacceptable treatment results. Studies were graded into effectiveness categories using prespecified criteria to objectively compare regimens using a Therapy Report Card similar to that used to grade the performance of school children. The intention to treat cure rate categories are: F or unacceptable (<80%), D or poor (80–84%), C or fair (85–89%), B or good (90–95%), and A or excellent (95–100%). The category of “excellent” was based on the cure rates expected with other prevalent bacterial infectious diseases.

**Results:** In the US and Europe recent (100 or greater subjects) large trials (total more than 2000 subjects) show that the triple therapy of a PPI + clarithromycin + amoxicillin has cure rates of F or less than 80% irrespective of duration. Sequential therapy scores as B.

**Conclusion:** Therapies that score “excellent” (grade = A) should be preferentially prescribed. B or “good” therapies can be used if “excellent” result are not obtainable. In most regions legacy triple therapy should be abandoned for unacceptable cure rates. Different quadruple therapies and sequential therapy are reasonable alternatives for initial therapy.

## 112

### Two Cases Involving Gastric Ulceration and Bleeding from Recent Placement of Gastrostomy Tubes with T-Fasteners

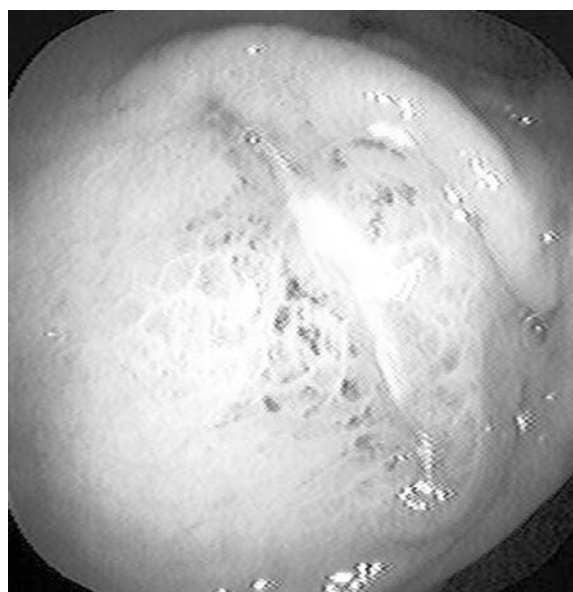
Rajesh Dhirmalani, DO, Dengda Tang, MD, Zamir Brelvi, MD\*. *Gastroenterology, UMDNJ, Newark, NJ.*

**Purpose:** The purpose of this case series is to elucidate an unforeseen complication related to (T-tacks) in the assistance of RIG and PIG.

**Results:** Both cases involved a 68 and an 82 yr CVA patients with recent placement of Gastrostomy tubes. T-tacks were used in both cases for gastropexy to aid in the introduction of the gastrostomy tubes. In both cases the patients returned to the ER with upper Gi bleeding 1–2 weeks post-gastrostomy placement. Both patients were resuscitated in the emergency department.

The 68 yr patient was endoscoped under conscious sedation. Endoscopic exam of the esophagus and duodenum was normal. The gastrostomy site was identified and the gastric bumper was noted to be in good position. Along side of the bumper were the retained T-tacks. One of the T-tacks was abutting into the gastric wall where an actively bleeding gastric ulcer was identified. The area was injected with epinephrine 1:10,000 mixture and biciped with good hemostats is. The t-tacks were then removed with a snare on a second sitting. The patient went home but did return with continued bleeding from the previous ulcer site. The patient was re-treated with Epi and bicap and hemostasis was maintained.

The 82 yr patient presented to the ER 3 weeks after the above patient with similar scenario. Endoscopy was performed that day and the gastrostomy site was identified. No erosions or ulcerations were identified in the antrum. Upon inspection of the gastrostomy site was the presence of two T-tacks with one buried into the gastric wall. There was surrounding edema and ulceration at the site. In this case the T-tacks were attached to the external bumper via suture material. The sutures were released from the bumper. Grasping forceps were then used to endoscopically remove the T-tacks from the gastric wall.[figure1][figure2]



## 113

### Optimizing the Detection of Fundic Gland Polyp Dysplasia in Subjects with Familial Adenomatous Polyposis

Laura K. Bianchi, MD, Ana E. Bennett, MD, Rocio Lopez, MS, Hennie Hasson, RN, Carol A. Burke, MD\*. *Gastroenterology, Cleveland Clinic, Cleveland, OH; Anatomic Pathology, Cleveland Clinic, Cleveland, OH and Quantitative Health Sciences, Cleveland Clinic, Cleveland, OH.*

**Purpose:** Dysplasia in fundic gland polyps (FGPs) is common in familial adenomatous polyposis (FAP) and gastric cancer is reported arising from FGPs in FAP. Optimal biopsy protocols are elucidated for dysplasia detection in IBD and Barrett's, but have not been investigated for dysplasia detection in FGPs in FAP. Our aim was to determine the most effective biopsy strategy for the detection of dysplasia in FAP FGPs.

**Methods:** A systematic protocol was utilized to biopsy FGPs from consecutive pts with FGPs undergoing routine endoscopic surveillance for FAP. FGP number (1–20, 21–30, >30) and size (1–4 mm, 5–10 mm, >10 mm) was recorded. The stomach involved with FGPs was visually divided into equal segments: proximal, middle, distal. Equal numbers of FGPs were biopsied from each segment. If 1–20 FGPs, 9 biopsies obtained. If 21–30 FGPs, 15 biopsies obtained. If > 30 FGPs, 21 biopsies obtained. Directed biopsies were obtained from large (>1 cm) and irregular appearing FGPs. One gastrointestinal pathologist blinded to the endoscopic findings interpreted all histology.

**Results:** 66 subjects (48% female) with a mean age of 43.6 yrs. 8% reported a family history of gastric cancer. Dysplasia was detected in 41% (2 subjects with high grade dysplasia (HGD), 25 subjects with low grade dysplasia (LGD)). 12% (3/25) had LGD in all three sets of polyps biopsied; 32% (8/25) had LGD in FGPs biopsied from the proximal segment; 52% (13/25) had LGD in FGPs from the middle segment, and 48% (12/25) with LGD in FGPs from the distal segment. Biopsies from proximal and middle segments missed 36% of subjects with LGD; biopsies from middle and distal segments missed 20% of LGD. 8% (2/25) of subjects with LGD were detected on directed biopsies alone. 100% (2/2) of subjects with HGD were detected in directed biopsies of large or irregular FGPs. 89% of subjects with dysplasia were detected by either directed biopsies of large or irregular FGPs or random biopsies from the distal 2/3 of the stomach.

**Conclusion:** LGD was not uniformly distributed among FGPs. HGD was detected only in directed biopsies. The yield for dysplasia detection was greatest when directed biopsies of large (>1 cm) and irregular FGPs were combined with random biopsies obtained from FGPs in the distal 2/3 of involved mucosa.

## 114

### Fundic Gland Polyp Dysplasia Is Common in Familial Adenomatous Polyposis

Laura K. Bianchi, MD, Ana E. Bennett, MD, Rocio Lopez, MS, Hennie Hasson, RN, Carol A. Burke, MD\*. Gastroenterology, Cleveland Clinic, Cleveland, OH; Anatomic Pathology, Cleveland Clinic, Cleveland, OH and Quantitative Health Sciences, Cleveland Clinic, Cleveland, OH.

**Purpose:** Fundic gland polyps (FGPs), common in Familial Adenomatous Polyposis (FAP), have been considered non-neoplastic, but gastric cancer is reported arising from them. This implies a dysplasia-carcinoma sequence, but the prevalence of FGP dysplasia has not been well studied. We sought to prospectively determine the prevalence of FGPs and FGP dysplasia in FAP via a systematic biopsy protocol and to identify endoscopic or demographic features associated with FGPs or FGP dysplasia.

**Methods:** Demographic and medical information (age, gender, race, family history of gastric cancer, exposure to tobacco, NSAIDs, or acid suppressive medications-PPI/H2RA) were obtained from consecutive FAP patients undergoing routine surveillance EGD. Endoscopic findings were recorded: FGP number (1–20, 21–30, >30), size (1–4 mm, 5–10 mm, >10 mm), duodenal polyposis stage, presence of H pylori. The stomach involved with FGPs was visually divided into equal segments: proximal, middle, and distal. Equal numbers of FGPs were biopsied from each segment. Directed biopsies were obtained from large (>1 cm) and irregular appearing FGPs. One gastrointestinal pathologist who was blinded to the endoscopic findings interpreted all histology.

**Results:** 75 subjects (52% male) with a mean age 44 yrs were included. 88% (66/75) of subjects had FGPs. H. pylori was detected in 33.3% of subjects without and 1.5% of subjects with FGPs ( $P = 0.005$ ). 38% (25/66) of subjects had LGD and 3% (2/66) had HGD. After adjusting for stage of duo-

denal polyposis, presence of antral gastritis, size of largest FGP and tobacco exposure, multivariable logistic regression analysis found PPI/H2RA use had a protective effect against FGP dysplasia (OR 0.15, 95% CI 0.02–0.95). Subjects with > 30 FGPs were 9.4 times more likely to have dysplasia than subjects with < 20 FGPs (OR 9.44, 95% CI 0.96, 92.55). For every increase in stage of duodenal polyposis the odds of having dysplasia nearly doubled (OR 1.91, 95% CI 0.87, 4.19).

**Conclusion:** The majority of FAP patients have FGPs and FGP dysplasia is common in FAP. There is a negative association between FGPs and presence of H pylori. FGP dysplasia is associated with increased number of FGPs and increased stage of duodenal polyposis. Use of acid suppressive medications has a protective effect against dysplasia in FGPs.

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### Effects of Cobiprostone on Indomethacin- and Stress-Induced Gastric Ulcers in Rats

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**Purpose:** This study was done to evaluate the ability of cobiprostone, a member of the prostone family of compounds which selectively activate type-2 chloride channels, to protect against indomethacin- and stress-induced gastric ulcer formation in Wistar rats. Another prostone compound, lubiprostone, accelerates recovery of tight junction potential in acutely injured porcine ileal mucosa.

**Methods:** In the indomethacin-induced ulcer model, fasted animals were orally given 1 of 4 dose levels of cobiprostone, or vehicle. Ten minutes after dosing, all rats received an oral dose of 20 mg/kg indomethacin. Six hours after indomethacin dosing, all animals were euthanized and the stomachs were removed and fixed. The maximum length of the longest axis of each individual ulcer was measured, and the ulcer index was calculated as the sum of the lengths of all ulcers per stomach. The effect of cobiprostone on the formation of stress-induced gastric ulcers was also investigated, utilizing a rat water-immersion model. Fasted animals received orally 1 of 3 doses of cobiprostone, 1 of 2 doses of lansoprazole, or a single dose of vehicle. Ten minutes after dosing, all animals were placed into a stress cage and vertically immersed in 23°C water up to the height of the xiphoid process. Five hours after the immersion, all animals were then euthanized and the stomachs removed and fixed. The ulcer index was calculated as stated above.

**Results:** The results from the indomethacin model indicate that 0.3, 1, 3, and 10 mcg/kg cobiprostone dose-dependently inhibited the generation of indomethacin-induced gastric ulcers by 2, 59, 65, and 77% vs vehicle, respectively; this inhibition was statistically significant at 1, 3 and 10 mcg/kg vs. vehicle ( $P < 0.01$ ). The stress study shows that 10, 30, and 100 mcg/kg cobiprostone dose-dependently inhibited the generation of stress-induced ulcers by 21, 36, and 85% vs vehicle, respectively. This inhibition was statistically significant at 100 mcg/kg vs vehicle ( $P < 0.01$ ). Lansoprazole, at concentrations of 1,000 and 10,000 mcg/kg, also dose-dependently and statistically significantly inhibited the generation of stress-induced ulcers by 37 and 95% vs vehicle, respectively ( $P < 0.01$ ).

**Conclusion:** The results of these studies indicate that cobiprostone can protect the stomach against the development of indomethacin- and stress-induced gastric ulcers. Furthermore, the cytoprotective effect against stress-induced gastric ulcers is at least 30-fold more potent than that of lansoprazole. This research was fully funded by Sucampo Pharmaceuticals, Inc.

## 116

### A Retrospective Study on the Role of Helicobacter pylori in Positive Fecal Occult Blood Tests in Hispanic Veterans

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**Purpose:** Fecal occult blood testing (FOBT) is the less expensive and more widely used method for screening for colorectal cancer, nevertheless upper gastrointestinal tract lesions can cause a positive FOBT, leading clinicians to evaluate the upper GI tract when a colonic cause is not identified. In Puerto Rico the prevalence of *H. pylori* infection in adults can exceed 80%. We hypothesized that a significant proportion of upper endoscopy findings in patients with positive FOBT could be a result of *H. pylori* infection.

**Methods:** The study consists of a retrospective analysis of the records of asymptomatic patients screened for colorectal cancer during years 2000–2005 that had undergone upper endoscopy as part of the evaluation of at least one stool positive for FOBT. CLOtest was used to assess the presence of *H. pylori* in all patients. Positive endoscopy findings were defined as: erosive gastritis, duodenal or gastric ulcers, and duodenitis.

**Results:** Study group consisted of 273 Hispanic patients (97%) male, with a mean age of 67 years old. Most common endoscopic findings were: erosive gastritis in 115/273 (42%) patients, gastric ulcers in 26/273 (10%), duodenal ulcers in 19/273 (7%) and gastric cancer in 3/273 (1%). 117 patients (42.8%) had a positive CLOtest. Among the patients with a positive CLOtest, the probability of upper endoscopy findings was higher [775.2% (88/117)] when compared to those with non-significant or negative findings [24.8% (29/117)]. ( $P = 0.001$ ). 137 (50%) patients of the initial study group were using either aspirin and/or NSAID's. When these patients were excluded, 35.3% (48/136) had a positive CLOtest, of which 37/48 (77.1%) had positive endoscopic findings and 11/48 (22.9%) had none. Again this difference was statistically significant ( $P$  value of 0.001).

**Conclusion:** Patients with a positive FOBT and documented *H. pylori* infection are more likely to have significant findings on upper endoscopy. This study suggests that *H. pylori* infection might be a significant cause of positive FOBT in patients with negative colonoscopy. Prospective studies should be conducted to determine the role of *H. pylori* infection and upper endoscopic examination in patients with positive FOBT.

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#### ***Okadaella gastrococcus*-like Immunoreactivity in Gastric Mucosal Lesions**

Takayuki Okada, MD, Kazutoshi Hori, MD, Kazuhiko Nakajima, MD, Hiroto Miwa, MD, FACP\*. Medicine, Okada Medical Clinic, Brisbane, QLD, Australia and Gastroenterology, Hyogo College of Medicine, Hishinomiya, Hyogo, Japan.

**Purpose:** Our previous reports on the nature of an intracellular gram-negative coccoid bacteria *Okadaella gastrococcus* (Og) and its association with various gastric mucosal lesions (GML) have been based on the findings from histochemistry, electron microscopy and culture. At present, transmission electron microscopy is the gold standard to visualize intracellular Og. The aim of this study was to examine if intracellular Og could be visualized in various GML by a newly developed Og immunohistochemistry.

**Methods:** The gastric biopsy specimens obtained at the time of esophago-gastro-duodenoscopy were used (total 8 patients; *Helicobacter pylori* (Hp) positive cases 2 and Hp negative cases 6). A rabbit polyclonal antibody against Og was raised by a standard method by Japan Biotest laboratory. Immunohistochemical detection of Og was performed on formalin-fixed, paraffin-embedded sections using an avidin biotin peroxidase complex technique. Polyclonal anti-Hp antibody (Dako) was used to visualize Hp.

**Results:** The heavily stained Og-like immunoreactivities (OGLIR) were detected in the mucous and the epithelial cells of gastric mucosa of active chronic gastritis, chronic gastritis, gastric erosions, and gastric ulcers including Hp-positive and Hp-negative cases. Positive OGLIR were also seen in the specimens with atrophy, intestinal metaplasia, dysplasia and malignancy including gastric MALT lymphoma.

**Conclusion:** The present novel Og immunohistochemistry could visualize intracellular and extracellular Og-like organism in various GML. Further studies are warranted to examine if those Og immunoreactive organisms are identical to the cultured Og utilizing the method such as immuno-electron microscopy or in situ hybridization.

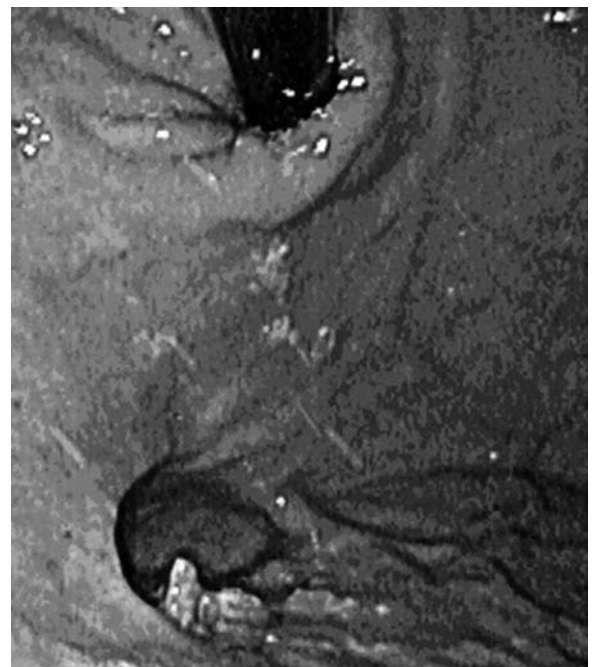
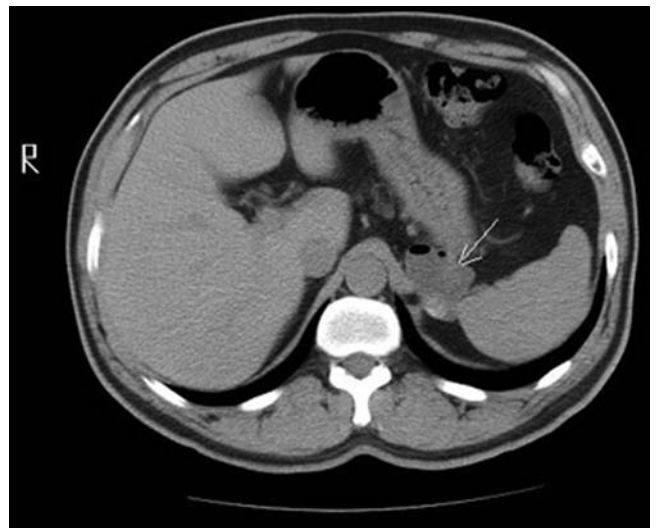
118

#### **Unusual Case of Gastric Diverticulum**

Alan Brijbassie, MD, Oswaldo Bisbal, MD\*. Gastroenterology Division, Salem VA Medical Center, Salem, VA.

**Purpose:** Diverticular disease is usually present in the large intestine; gastric diverticulosis on the other hand is very rare. We now present the case of what was believed to be an adrenal adenoma, however endoscopically proven to be a gastric diverticulum.

A 60 year old Caucasian male presented with a three month history of left sided abdominal pain and gastroesophageal reflux. CT of the abdomen revealed a left sided adrenal region mass exhibiting air fluid level (white arrow on CT). Upper endoscopy was performed, revealed a 2 cm diverticulum in the gastric fundus.



Gastric diverticular disease is a uncommon disease with endoscopic detection rates ranging between 0.01–0.11%. The majority (up to 75%) form near the gastroesophageal junction, usually on the lesser curvature or posterior gastric wall. Gastric cardia diverticuli may simulate a left adrenal mass;



those of the posterior wall can herniate through an area of dorsal mesentery and fuse with the left posterior body wall. If the latter form occurs during organogenesis, they can indent Gerota's fascia and dissect between the left adrenal gland and kidney. Size ranges from 1–3 cm, however larger sizes have been reported. The majority remains asymptomatic however perforation, bleeding, aggravation of esophageal reflux and cancer formation have been reported. Though uncommon, gastric diverticular disease can be a significant cause of morbidity if complications occurs and should be part of the differential diagnosis when investigating upper gastrointestinal symptoms.

**Methods:** Bibliography 1. Schweiger F, Noonan J: An unusual case of Gastric Diverticulosis: American Journal of Gastroenterology 1817–1819, 1991 2. Thomschke D, Gockel I, Lorenz D: Gastrointestinal: Gastric Diverticula: Journal of Gastroenterology and Hepatology 227–228, 2004 [figure1][figure2]

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### Effect of Prokinetics (PK) on Gastric Emptying (GE) and Symptoms in Placebo-Controlled Trials of Gastroparesis: A Systematic Analysis

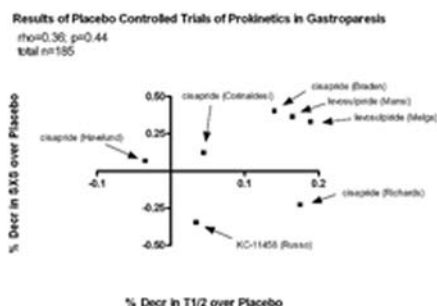
Preet Bagi, MD, Michael D. Crowell, PhD, Nicholas J. Talley, MD, Michael P. Jones, MD\*. Division of Gastroenterology, Northwestern University, Chicago, IL; Division of Gastroenterology, Mayo Clinic, Rochester, MN and Division of Gastroenterology, Mayo Clinic, Scottsdale, AZ.

**Purpose:** PK are typically given to pts with sx attributed to abnormal GE. However, the relationship between sx and GE is poor and most studies have methodological limitations. To better understand PK efficacy in the treatment of pts with abnormal GE, we conducted a systematic literature review.

**Methods:** MEDLINE, MeSH and Cochrane databases were searched for RCTs in adults published prior to 5/07. Primary search terms were “gastroparesis,” “prokinetic,” as well as specific PKs. Included trials were  $\geq 2$  wks, placebo-controlled (PLA) and used validated GE methods. Studies without raw data were excluded. Changes in sx and GE rates were calculated for PK and PLA as the difference between BL and treatment scores.

**Results:** 14/92 identified studies met inclusion criteria. 7/14 included BL and post-treatment sx and GE assessment: cisapride(4); levosulpiride(2) and motilin against KC 11458(1). 7/14 met inclusion criteria but did not measure GE after treatment: cisapride(1); metoclopramide(4) and motilin agonist ABT-229(2). The trials included 685 pts with 185/685 in studies reporting BL and post-treatment sx and GE. Median (95% CI) percent change in sx from BL for PLA was 27%(18–38%). Median net therapeutic gain of PK over PLA for sx scores from BL was 20%(–0.04–34%). Median net therapeutic gain for indiv PK classes was 12% for cisapride/levosulpiride, 32% for metoclopramide and 2% for motilin agonists (Fig.). PLA was assoc with a 7%(3–13%) improvement in GE rate and net therapeutic gain of PK over PLA for improvement in GE rates was 14%(4–18%). The correlation ( $r_s$ ) of net therapeutic change in sx scores with net therapeutic change in GE rate was 0.36( $P = 0.44$ ).

**Conclusion:** There are limited data to support the concept that improving GE improves attributed sx. The greatest sx relief occurs with agents that also exert central antiemetic effects. Pure PK such as motilin agonists offer little beyond PLA for sx improvement. The clinical utility of GE studies requires critical reappraisal.[figure1]



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### Expression of MUC5AC and TFF1 in Intestinal Metaplasia Subtypes

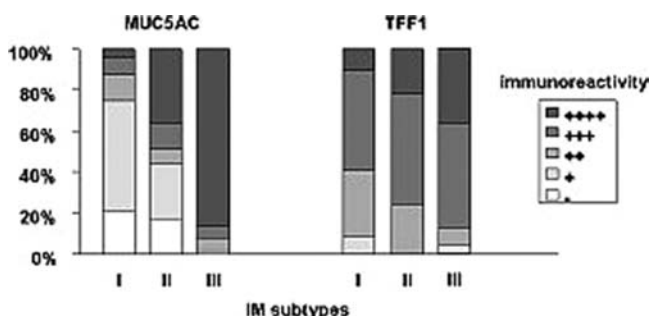
Byung Wook Kim, MD, Lee-So Maeng, MD, Kyoung-Mee Kim, MD, In-Sik Chung, MD\*. Internal Medicine, The Catholic University of Korea, Seoul, Republic of Korea and Pathology, The Catholic University of Korea, Seoul, Republic of Korea.

**Purpose:** Several studies have shown that type III intestinal metaplasia (IM) is associated with an increased risk of malignant transformation. In other studies, alterations of the expression pattern of mucins and trefoil peptide have been described in carcinomas as well as in their precursor lesions. The aim of this study was to evaluate the expression of MUC5AC and TFF1 in different subtypes of IM.

**Methods:** Endoscopic gastric biopsies at antrum and body were obtained from 70 patients with functional dyspepsia and endoscopic IM. Alcian blue (pH2.5)/periodic acid-Schiff and the high iron diamine technique were used to classify the subtypes of IM. Immunoreactivity for MUC5AC and TFF1 was observed in different types of IM.

**Results:** IM was detected in 136 samples. Type I was detected in 47 samples, type II in 40 samples, and type III in 49 samples. MUC5AC and TFF1 are highly expressed in incomplete IM (Fig.).

**Conclusion:** Type II and type III IM seems to be more common in Koreans than in Westerns. This may be associated with high incidence of gastric cancer in Koreans. MUC5AC and TFF1 expression may not be coexpressed in any of the different types of IM.[figure1]

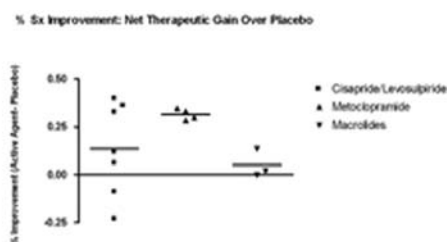


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### Clinical Presentation and Endoscopic Management of Dieulafoy's Lesions in an Urban Community Hospital

SriKrishna Nagri, Sury Anand, Yashpal Arya\*. Gastroenterology, Brooklyn Hospital Center, Brooklyn, NY and Gastroenterology, Wyckoff Heights Medical Center, Brooklyn, NY.

**Purpose:** Dieulafoy's lesion consists of a small sub-mucosal artery that protrudes through a tiny mucosal defect and is an uncommon but important cause of major gastrointestinal bleeding. The aim of this retrospective study



was to identify rates of occurrence, common clinical and endoscopic features and to review the outcome of endoscopic management of Dieulafoy's lesions in the upper GI tract in an urban community hospital setting.

**Methods:** Endoscopic data from EGDs done at Wyckoff Heights Medical Center, Brooklyn, NY between 2000 and 2006 were reviewed to identify patients with Dieulafoy's lesions. Demographic data, medical history, examination findings, lab data, endoscopic findings and details of therapy for these 15 patients treated for Dieulafoy's lesions were reviewed retrospectively.

**Results:** Dieulafoy's lesions were documented to be the cause of bleeding in approximately 1% of patients presenting with gastrointestinal bleeding while they were detected in only 2 patients when the indication was other than active GI bleeding. When we analyzed EGDs performed in patients above age 65 presenting with gastrointestinal bleeding, prevalence approached 10 percent. The most common location of the lesion was the body of stomach (seven), followed by the cardia (four) and the esophagus (two). One patient had this lesion in the fundus and one patient in the duodenal apex. All the patients were initially treated endoscopically with epinephrine injection, in eight cases heater probe was applied following epinephrine and endoscopic clips were applied in two cases. All but one of the patients did well in near and intermediate term follow-up (Average follow-up period of 18 months). One patient died of multi-organ failure during the same hospital stay. Average length hospital stay was 7 days.

**Conclusion:** Community hospital gastroenterologists and endoscopists should be aware that Dieulafoy's lesions are a not so uncommon cause of upper GI bleeding among elderly patients. It accounted for 10% of acute upper GI bleeding in elderly in our study. Early accurate diagnosis through emergent endoscopy and endoscopic therapy, especially in patients with multiple co-morbid conditions, is very effective and life saving.

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#### Contained Duodenal Perforation Manifesting as a Cystic Mass Can Be Managed Non-Surgically

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**Purpose:** Perforation of duodenal ulcer presents as an acute abdomen, with diffuse peritonitis. We report a rare case of contained duodenal perforation that was managed nonsurgically.



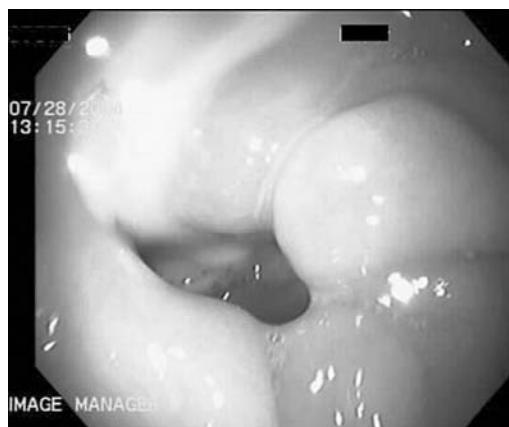
**Case report:** A 48 year old female with chronic back pain on rofecoxib and ibuprofen presented with epigastric pain radiating to the right abdomen for 2 weeks, emesis and low grade fever. She had a 20 pack year history of cigarette smoking and drank 2 beers a day. Examination revealed a hemody-

namically stable, febrile patient with epigastric tenderness but no guarding. There was no ascites and the bowel sounds were normal.

**Work-up:** Blood work was unremarkable except for leucocytosis. There was no pneumoperitoneum on X-ray. CT scan showed 7.3 × 6.5 × 4.6 cm cystic mass adjacent to the pancreas. EGD showed purulent discharge from an ulcer bed in the anterior wall of the duodenal bulb and extrinsic compression of the duodenum. Antral biopsies showed no evidence of *H. pylori*.

**Management:** She was kept nil by mouth and started on nasogastric suctioning; treated with intravenous proton pump inhibitor and broad spectrum antibiotics; and was closely followed by surgeons. She recovered without complications in 1 week.

**Conclusion:** This case highlights the following points: Consider perforated duodenal ulcer whenever there is inflammatory cystic mass in relation to the head of pancreas. Endoscopy confirms diagnosis in such cases. Although most patients with perforated duodenal ulcer require surgical closure, patients with a contained perforation could be managed successfully without surgery.[figure1][figure2]



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#### Case Report: Zantac 300 mg BID Controls Gastric Acid Secretion vs Nexium 75 mg BID in a Patient with Gastric Bypass and Clinically Significant Vomiting

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**Purpose:** This is a 48-year-old female who has had a Roux-en-y gastric bypass, with an anastomotic ulcer causing pain and vomiting, which precludes adequate nutrition. She is on TPN with a venting PEG tube surgically placed. The patient has had a recent onset of epigastric pain and vomiting. Our aims were: 1) To assess 24-h baseline gastric acidity in the stomach, 2) To compare Zantac 300 mg BID and Nexium 40 mg BID regarding control of gastric acidity, and 3) To assess symptom improvement on both regimens.

**Methods:** Patient was scheduled for three 24-h gastric pH-monitoring sessions at least 10 days apart: baseline, after 5 days of Nexium 40 mg BID, and during 1st day dosing with Zantac 300 mg BID. The dual pH probe was advanced into the stomach across the PEG tube at 20 cm so that both sensors were placed in the stomach. During each pH monitoring, patient consumed her usual small meals throughout the day and underwent her usual 16-h TPN feedings from 1800 to 1000 the next morning.

**Results:** Patient had 3 episodes of vomiting while off acid suppressive medication. Acid was present throughout the 24-h, with mean pH of 1.5 and 2.0 (sensors 1, 2). The gastric pH was above 4 for 0 and 6% of the time (sensors 1, 2). Although only 1 episode of vomiting was reported, Nexium did not alter mean gastric pH (1.1 and 1.8; sensors 1, 2), with 0 and 10.3% of the time pH > 4 (sensors 1, 2). After BID dosing with Zantac 300 mg, 2 episodes of vomiting occurred, and mean 24-h gastric pH was increased to 2.6 and

2.8. Gastric pH > 4 for 61.7 and 69.7% of the time. During TPN infusion, gastric pH > 4 for 0 and 8% of the 16 hour period during baseline, 0 and 14% on PPI, with an increase to 24 and 4% of the time on Zantac. While off TPN, gastric pH was > 4 for 0 and 2% of the time on no acid suppression, 0 and 3% of the time on PPI and increased to 68 and 83% on Zantac.

**Conclusion:** Although TPN increases gastric acid production and decreases gastric pH as evidenced by baseline 24-h gastric acidity, BID dosing with Zantac 300 mg, and not Nexium 40 mg BID, improves gastric acidity in this patient. This suggests that 1) surgical alteration of the stomach so that food bypasses the stomach dampens the meal-related acid secretion that is necessary for maximal PPI effect; 2) H2RA's which do not depend on food-induced burst acid secretion are more effective in this patient; and 3) pain is likely due to secondary ischemic anastomotic stricture and not acid induced.

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### Fasting Gastric Leptin Levels Are Elevated in Diabetics Independent of BMI

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**Purpose:** Leptin produced by adipocytes is involved in the regulation of weight as well as energy expenditure. Leptin is also produced by the gastric epithelium and may play a role in metabolism. The association of gastric leptin with diabetes has not been evaluated in humans. Our aim was to evaluate both plasma and gastric leptin levels in diabetics compared to non-diabetics.

**Methods:** Patients referred for upper endoscopy were prospectively enrolled after a 12-hour overnight fast. Patients with documented Hemoglobin A1C levels >5 were classified as diabetic (DB+), while all other non diabetics (DB-) served as controls. A detailed medical history, height, and weight were obtained, and BMI was calculated. Serum was collected, and biopsies were obtained from the antrum, and fundus. Leptin levels in plasma and gastric biopsy samples were determined by specific ELISA, and gastric concentrations were normalized according to biopsy protein (pg/mg protein). To avoid confounding due to *H. pylori*'s known effect on gastric leptin, *H. pylori*+ individuals were excluded from further analysis.

**Results:** Among the 278 enrolled individuals 169 (60%) tested *H. pylori*+ and were excluded. Among the 101 *H. pylori* negative individuals; 20 were diabetic (DB+) with mean age of  $66 \pm 10$  years and 81 were non-diabetic (DB-) with mean age of  $63 \pm 12$  years. The mean BMI was significantly higher in the DB+ group compared to the DB- group ( $31 \pm 5$  vs.  $28 \pm 5$ ,  $P = 0.003$ ). Although it was correlated with BMI ( $r = 0.59$ ,  $P < 0.001$ ), plasma leptin levels did not differ significantly between the DB+ and DB- groups. Antral leptin also correlated with BMI ( $r = 0.23$ ,  $P = 0.024$ ) but levels were significantly higher in the DB+ compared to the DB- group (median 127 pg/mg IQR (50–173) vs. 105 pg/mg (68–244);  $P = 0.006$ ). The positive association remained significant in a multivariate logistic regression analysis controlling for age, sex, ethnicity, and BMI ( $P = 0.029$ ).

**Conclusion:** Plasma leptin is correlated with BMI but does not distinguish diabetics from non-diabetics. In contrast, antral leptin is elevated in diabetics independent of BMI. Further evaluation of the role of gastric leptin and its receptor in regulating the energy expenditure of diabetics is warranted.

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### Gastric Lymphoma: The Vanishing Act

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**Purpose:** Spontaneous regression (SR) is a well-known phenomenon of various cancers, especially low-grade malignancies, and is referred to the disappearance of cancer cells without specific anti-cancer therapy. Diffuse large B cell lymphoma (DLBL) is an aggressive malignant neoplasm that can be fatal if left untreated. We report a case of SR of a gastric DLBL which is considered to be an extremely rare occurrence.

**Case Presentation:** A 40 year-old man, with a history of HIV, EBV, and CMV infections presented with abdominal pain, nausea and vomiting. Endoscopic examination (EGD) revealed a deep ulcer in the anterior wall near the antrum of the stomach, and an adjacent 5-mm satellite nodule. The patient's ulcer had perforated through the bowel wall and adhesions with the liver capsule were noted. Biopsy of the gastric ulcer and nodule showed diffuse infiltrate of immature large lymphocytes, positive for CD20, BCL6 and lambda light chains, and negative for CD3 and kappa that were diagnostic for DLBL. Bone marrow biopsy was negative and a nuclear scan showed uptake only at the gastric ulcer region. One month after the EGD biopsy, a subtotal gastrectomy was performed and the entire gastrectomy specimen and all possible lymph nodes were submitted for histopathological analysis. Immunohistochemistry stains for *Helicobacter pylori*/EBV/CMV antigens were all negative in both biopsy and gastrectomy specimens. Intriguingly, no residual lymphoma was identified anywhere in the gastrectomy specimens. PCR DNA profiling confirmed that the EGD biopsy and the gastrectomy specimens were from the same patient. During the 1 month period between the biopsy and gastrectomy, the patient had only received daily Omeprazole, 11 days of antidepressant drugs, and 3 days of Acyclovir for a herpes skin infection.

**Discussion:** SR of gastric DLBL is considered to be extremely rare and prior such reported cases involved use of either eradication therapy for *H. pylori* or histamine-2 receptor antagonists. None of these were used in our patient. Various humoral and immune-regulatory mechanisms, including the induction of an immune response secondary to trauma resulting from biopsies have been proposed to explain the concept of SR of cancers, but the topic is widely speculative even today.

**Conclusion:** Further elucidation of the process of SR might offer the possibility of finding a cure even for aggressive cancers with currently fatal outcomes.

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### Cobiprostone Is a Type-2 Chloride Channel Activator That Protects Against NSAID-Induced Cellular Damage

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**Purpose:** Cobiprostone is being clinically tested as a protectant against non-steroidal anti-inflammatory drug (NSAID)-induced ulcers, and the present study is to determine the cellular and molecular basis of protection by cobiprostone against NSAID-induced cellular damage.

**Methods:** T84 cells were grown to confluence on solid supports. The effects of cobiprostone on indomethacin-induced changes in intracellular  $\text{Ca}^{2+}$  levels ( $[\text{Ca}^{2+}]_i$ ) using Indo-1/AM (a dye that measures  $[\text{Ca}^{2+}]_i$ ), and the effects of cobiprostone on mitochondrial membrane potential using JC-1 (a dye that monitors mitochondrial membrane potential), were tested. The effects of cobiprostone on indomethacin-induced cytochrome c release, cyclic AMP, and cell death and regrowth were also investigated.

**Results:** Five hundred (500)  $\mu\text{M}$  indomethacin caused an immediate increase in  $[\text{Ca}^{2+}]_i$ , which became irreversible (calcium deregulation) after approximately 30 minutes. One hundred (100) nM cobiprostone was shown to protect against indomethacin-induced increases in  $[\text{Ca}^{2+}]_i$ , and caused a reversal of indomethacin-induced calcium deregulation. However, cobiprostone did not prevent or reverse the increase in  $[\text{Ca}^{2+}]_i$  caused by indomethacin in the presence of different  $\text{Cl}^-$  channel blockers, including diphenylamine-2-carboxylate (DPC), niflumic acid or 4,4'-diisothiocyanatostilbene-2,2'-disulfonic acid (DIDS), suggesting that the protective effects of cobiprostone are due to activation of  $\text{Cl}^-$  channels.

Cobiprostone has only a small effect on cAMP levels in T84 cells, precluding a role of cAMP in the protective action of cobiprostone. Indomethacin caused depolarization of the mitochondrial membrane potential. Cobiprostone protected against indomethacin-induced depolarization of mitochondrial membrane potential and reversed the loss of mitochondrial membrane potential. Cobiprostone was also shown to protect against cytochrome c relocation from mitochondria into the cytoplasm, which is associated with apoptosis. Finally, in a novel long-term assay using T84 cell cultures, cobiprostone reduced indomethacin-induced cell death and promoted cell regrowth.

**Conclusion:** Activation of  $Cl^-$  channels may underlie the protective effects of cobiprostone in protection against NSAID-induced damage. The results further indicate that cobiprostone has the potential to be of benefit against NSAID-induced cell death.

This research was funded entirely by Sucampo Pharmaceuticals, Inc., Bethesda, MD.

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### Is There Improvement over Years in the Diagnostic Accuracy of Endoscopic Ultrasound in Evaluating T-Staging of Gastric Cancers? A Meta-Analysis and Systematic Review

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**Purpose:** Prognosis and modality of treatment in patients with gastric cancers depends on the tumor T-staging, particularly with the emerging of novel endoscopic therapeutic modalities such as endoscopic submucosal dissection. The published data on the effect of changes in Endoscopic Ultrasound's (EUS) technology over time on the accuracy of T-staging in patients with gastric cancers have been varied.

**Aim:** To evaluate the affect of EUS technology over accuracy in T staging of gastric cancers.

**Methods: Study Selection Criteria:** Only EUS studies confirmed by surgery were selected. EUS criteria used for T staging were: T1- the tumor invades the lamina propria or submucosa, T2- the tumor invades but does not extend beyond the muscularis propria, T3- the tumor invades the perigastric tissues, and T4- the tumor invades adjacent structures.

**Data collection & extraction:** Articles were searched in Medline, Pubmed, Ovid journals, and Cochrane control trial registry. Two reviewers independently searched and extracted data.

**Statistical Method:** Meta-analysis for the accuracy of EUS was analyzed by calculating pooled estimates of sensitivity, specificity, likelihood ratios, and diagnostic odds ratio. Pooling was conducted by both the fixed and random effects models.

**Results:** Initial search identified 1,620 articles, of these, 360 relevant articles were selected and reviewed. 20 studies (N = 1750) which met the inclusion criteria were included in this analysis. Pooled accuracy data for T staging

over last two decades is shown in table 1. All the pooled estimates calculated by fixed and random effect models were similar. The *P* for chi-squared heterogeneity for all the pooled accuracy estimates was >0.10.

**Conclusion:** EUS has excellent sensitivity and specificity in accurately diagnosing the T-stage in a patient with gastric cancer. Over the last two decades, a significant improvement were noted in the specificity and sensitivity of EUS in diagnosing the early (T1) stage of the tumor. EUS should be strongly considered for T staging of gastric cancers.[figure1]

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### Endoscopic Ultrasound's Diagnostic Accuracy in Detecting Distal Metastasis of Gastric Cancers: A Meta-Analysis and Systematic Review

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**Purpose:** Distal metastasis in patients with gastric cancer predicts prognosis and guides therapy. The published data on accuracy of endoscopic ultrasound (EUS) for diagnosing distal metastasis (M1) in patients with gastric cancers has been inconsistent.

**Aim:** To evaluate the accuracy of EUS in diagnosing distal metastasis of gastric cancers.

**Methods: Study Selection Criteria:** Distal metastasis was defined as metastasis to peritoneum, liver, cervical lymph nodes, celiac axis lymph nodes, or abdominal lymph nodes.

**Data collection & extraction:** Articles were searched in Medline, Pubmed, Ovid journals, and Cochrane control trial registry. Two reviewers independently searched and extracted data.

**Statistical Method:** Meta-analysis for the accuracy of EUS was analyzed by calculating pooled estimates of sensitivity, specificity, likelihood ratios, and diagnostic odds ratios. Pooling was conducted by both fixed and random effects models. The heterogeneity of studies was tested using Cochran's *Q* test based upon inverse variance weights.

**Results:** Initial search identified 3630 reference articles, in which, 346 relevant articles were selected and reviewed. Four studies met the inclusion criteria and data for EUS accuracy to diagnose distant metastasis was extracted from those studies. The pooled sensitivity to diagnose distal metastasis was 73.2% (95% CI: 63.2–81.7). EUS specificity was 88.6% (84.8–91.7). The positive likelihood ratio to diagnose distal metastasis was 17.2 (2.8–106.3) and the negative likelihood ratio was 0.4 (95% CI: 0.2–0.7). The diagnostic odds ratio of EUS to correctly diagnose distal metastasis was 60.9 (95% CI: 8.2–463.7). The SROC curve showed an AUC of 0.98 with a standard error (SE) of 0.005. This curve showed a *Q* value of 0.94 with a SE of 0.0. All the pooled estimates, calculated by fixed and random effect models, were similar. The *P* for chi-squared heterogeneity for all the pooled accuracy estimates was >0.10.

Table 1: Accuracy of EUS with confidence intervals to stage esophageal cancers over the past two decades

		No. of Studies	Pooled Sensitivity	Pooled Specificity	Pooled LR+	Pooled LR-	Pooled DOR
T1	1906 to 1994	12	56.3 % (49.7 - 62.6)	89.1 % (85.5 - 92.1)	4.6 (1.6 - 13.8)	0.51 (0.38 - 0.69)	9.3 (2.9 - 30.1)
	1995 to 1999	4	82.2 % (67.9 - 92.0)	100.0 % (87.9 - 100.0)	72.9 (16.2 - 288.8)	0.13 (0.03 - 0.68)	562.5 (62.0 - 3438.4)
	2000 to 2006	5	84.8 % (71.1 - 93.7)	100.0 % (88.9 - 100.0)	88.9 (25.3 - 312.4)	0.22 (0.13 - 0.38)	428.9 (66.6 - 1904.8)
T2	1906 to 1994	12	84.9 % (79.8 - 89.2)	96.7 % (95.4 - 97.8)	20.5 (14.8 - 28.4)	0.19 (0.13 - 0.30)	207.0 (109.5 - 391.8)
	1995 to 1999	4	74.4 % (57.9 - 87.0)	90.9 % (85.4 - 94.8)	6.7 (2.5 - 18.1)	0.33 (0.19 - 0.56)	23.7 (5.3 - 106.2)
	2000 to 2006	5	79.5 % (70.8 - 86.5)	94.6 % (91.3 - 96.9)	16.8 (5.3 - 53.8)	0.22 (0.12 - 0.38)	79.6 (22.9 - 277.2)
T3	1906 to 1994	12	89.6 % (86.3 - 92.3)	95.3 % (93.6 - 96.7)	15.5 (11.4 - 21.1)	0.12 (0.07 - 0.22)	160.2 (95.5 - 268.7)
	1995 to 1999	4	90.3 % (80.1 - 96.4)	91.3 % (85.8 - 95.2)	11.1 (3.5 - 35.4)	0.12 (0.06 - 0.25)	93.3 (30.6 - 264.6)
	2000 to 2006	5	89.8 % (83.3 - 94.5)	94.8 % (91.3 - 97.2)	13.9 (7.7 - 25.1)	0.12 (0.04 - 0.37)	154.7 (55.7 - 429.5)
T4	1906 to 1994	12	88.9 % (85.9 - 91.9)	97.1 % (95.9 - 98.0)	23.3 (14.6 - 37.4)	0.07 (0.04 - 0.14)	626.4 (256.1 - 1532.5)
	1995 to 1999	4	100 % (92.5 - 100.0)	95.8 % (91.5 - 99.3)	14.3 (7.6 - 26.9)	0.05 (0.01 - 0.18)	441.7 (85.6 - 2279.1)
	2000 to 2006	3	100.0 % (87.2 - 100.0)	96.7 % (91.9 - 99.0)	16.4 (7.9 - 33.9)	0.07 (0.02 - 0.33)	260.1 (43.7 - 1547.4)

LR+ = Positive Likelihood Ratio  
LR- = Negative Likelihood Ratio  
DOR = Diagnostic Odds Ratio

**Conclusion:** For distant metastasis, though the number of studies with data was smaller, the pooled specificity is high but the sensitivity is not as high. Though EUS is not designed to detect all areas of distal metastasis, improvements in technology or diagnostic criteria are needed to enhance the sensitivity.

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### Incidence of Endoscopic Gastric and Duodenal Ulcers (GDUs) in Randomized Placebo-Controlled NSAIDs Trials: A Meta-Analysis

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**Purpose:** GI safety of NSAIDs is often evaluated by comparison with placebo in clinical trials. The incidence of GDUs in placebo arms may reflect background noise and influence interpretation of the relative safety of NSAIDs. We investigated the incidence of GDUs in placebo-controlled NSAIDs trials over three decades.

**Methods:** Randomized placebo-controlled trials of NSAIDs from 1975 to 2006 were systematically reviewed. Trials required endoscopy before and after treatment.

**Results:** Thirty-six studies met inclusion criteria with treatment duration of 6.5 days to 24 weeks. 3.43% (98/2861) GDUs were reported in placebo arms overall [1.04% in healthy volunteers (HV) vs. 3.93% in OA/RA patients,  $P = 0.002$ ]. GDU rate in placebo arms was 0 (0/83), 4.20% (35/833), and 3.24% (63/1945) in studies from 1975–1989, 1990–1999 and 2000–2006, respectively ( $P > 0.05$ ). In univariate analysis, pooled ulcer rate on placebo was significantly higher in studies with mean age  $\geq 60$  yr (4.14% vs 2.59%); treatment duration  $\geq 4$  weeks (3.85% vs 0.95%); OA/RA patients vs HV (3.93% vs 1.04%); patients with previous GI events (4.12% vs 0.83%); subjects with  $<10$  mucosal erosions at baseline vs normal mucosa (3.85% vs 1.13%) ( $P < 0.05$ ). No significant difference was seen with cotherapy with vs. without low-dose aspirin/corticosteroids (3.79% vs 2.64%). 11.85% ( $N = 8125$ ) GDUs were reported in all NSAIDs (nsNSAIDs + coxibs + CINOD) treated subjects (68 arms) from 1990 to 2006, and GU rate was 3-fold higher than DU (8.48% vs 2.84%). GDU rate in all NSAIDs users declined after 2000 (13.26% vs 11.33%); the decrease of GDUs in nsNSAIDs users was significant (20.08% vs 15.82%); no significant change was seen with coxibs. Overall, the incidence of GDUs in nsNSAIDs arms (17.06%) was significantly higher than in coxib (5.00%) or placebo arms (3.43%); GDU rate in coxib arms was significantly higher than in placebo (5.00% vs 3.43%) ( $P < 0.05$ ).

**Conclusion:** Endoscopic GDU rate in placebo arms has not changed over the last 3 decades. Treatment duration, previous GI events, age and baseline mucosal damage are associated with increased GDUs. GU was predominant in NSAIDs-associated ulcers. nsNSAIDs are associated with a higher GDU rate than placebo or coxibs, regardless of risk factors. The GDU rate significantly decreased after 2000, which may be due to increasing coxib use for high risk patients, and also because high risk patients are no longer randomized to clinical trials.

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### Syndrome Dyspepsia in the Population of Jakarta Indonesia

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**Purpose:** One third of patients who go to the medical practitioners, and half of the patients who go to the gastroenterologist have this syndrome dyspepsia.

The purpose of this study is to know the epidemiology of syndrome dyspepsia in the population of Jakarta Indonesia and other factors related to syndrome dyspepsia.

**Methods:** This epidemiological study was done with interview method to 1645 patients that represent all of the Jakarta's population. The selection of patients using the cluster random sampling in which every area represented by one area and the patient was interviewed randomly. Syndrome dyspepsia was defined if there are symptoms of epigastric pain and epigastric discomfort lasting for more than 1 month. Analysis was done by stata program after corrected with the certain factor. Interview was done on every selected patient after being given informed consent by the person who were in charge to do the interview and by signing the consenting form.

**Results:** The proportion of syndrome dyspepsia was 58.1%. The most frequent patient in syndrome dyspepsia was female 59.1%, mean of age  $44.05 \text{ yo} \pm 10.72$  years. The frequent symptom were nausea 30.1%, epigastric pain 28.7% etc. In the dyspeptic patients, 25.85% patients has a smoking habit, 2.58% patients consumed alcohol. There was a trend to get syndrome dyspepsia in patients who have anxiety, depression, who consumed NSAID ( $P = 0.000$ ).

**Conclusion:** The proportion of syndrome dyspepsia in Jakarta population was 58.1%. Syndrome dyspepsia was more frequent in female, who has anxiety, depression and who consumed NSAID.

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### A Cost Analysis of GERD and Dyspepsia in Iran

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**Purpose:** Gastroesophageal reflux disease and dyspepsia are both highly prevalent conditions and cause considerable health care utilizations and costs. The main goal of this study was to evaluate the health care utilizations and costs of these two gastrointestinal diseases in Iran.

**Methods:** A consecutive sample of 501 patients who referred for upper endoscopy to a private outpatient gastroenterology clinic in central Tehran was investigated if they have gastroesophageal reflux disease (having heartburn or regurgitation on a weekly basis for at least the past 3 months with symptom onset at least 12 months prior to the study) or dyspepsia (based on Rome II criteria) from May 2005 to January 2006. Then a questionnaire were filled for GERD and dyspepsia patients to determine the frequency of health resource utilization (physician visit, hospitalization, laboratory tests, imaging studies, and drugs) and productivity loss (days off work or with low functionality) due to related symptoms in the past 12 months. Societal perspective was used and cost per person per year was estimated in purchasing power parity dollars (PPPs).

**Results:** The cost of disease per person per year for patients who had only GERD, only Dyspepsia, and both GERD and dyspepsia were about 271.40, 286.90, and 408.10 PPP\$ respectively. There was no statistically significant difference in the cost of disease per person per year among patients having only GERD, only dyspepsia, and both GERD and dyspepsia. The direct cost of disease included 63.50%, 61.38%, and 46.98% of total cost among patient who had only GERD, only dyspepsia, and both GERD and dyspepsia respectively while cost of chemical drugs and imaging tests were the largest parts of it. There was also no statistically significant difference in cost of disease between GERD patients having esophagitis or not.

**Conclusion:** GERD and dyspepsia are associated with a considerable health economic burden to society considering their high prevalence in the population. As medication is the dominant cost factor, more investigation to find the best treatment strategy seems extremely necessary for decreasing the costs.

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### Survival in Gastric Cancer Patients: Univariate and Multivariate Analysis

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**Purpose:** The aim of this study was to analysis the survival of patients diagnosed with gastric cancer and the factors which modify prognosis.

**Methods:** Retrospective cohort study was performed on total patients diagnosed with gastric cancer registered in the Taleghani hospital cancer registry (Tehran, Iran) between 21 December 2001 and 21 December 2006. Information about demographic and clinical variables were gathered from the cancer registry forms and patients were followed up by telephone contact. The Kaplan-Meier statistical method was employed to determine the probability of survival and log-rank test to compared those. Cox regression was used to determine prognosis factors.  $P < 0.05$  was considered as statistically significant. All calculations was carried out by SPSS (version 13.0) statistical software.

**Results:** Of 746 patients, 38.6% were dead. The mean and median survival time was 42.45 and 22.8 months, respectively and five-year survival rate was 25.3%. With univariate analysis, Age at Diagnosis, type of treatment, type of first treatment, pathologic stage, tumor size, histology type, pathologic primary tumor and pathologic distant metastasis were significant prognostic factors related to overall survival time. Tumor size greater than 35 mm ( $HR = 2.12$ ) and have a metastasis ( $HR = 2.04$ ) were found to be the statistically significant poor prognostic factors related to survival in multivariate analysis.

**Conclusion:** According to results, early detection of cancer in lower ages and in primary grades of tumor, is important to increase patient's life expectancy.

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#### Assessment of Reasons for Non-Adherence to Nonvariceal Upper Gastrointestinal Bleeding (NVUGIB) Guidelines

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**Purpose:** Nonvariceal upper gastrointestinal bleeding (NVUGIB) causes substantial morbidity and mortality. Guidelines for the management of patients with NVUGIB exist, but are inconsistently applied by healthcare providers, resulting potentially in sub-optimal care and patient outcomes. A needs assessment was carried out to assess healthcare providers' barriers to the implementation of these guidelines in Canada.

**Methods:** Semi-structured key informant interviews were conducted by telephone with a sample of 22 selectively sampled healthcare professionals actively practicing with NVUGIB patients, including emergency room physicians [ER], intensivists [ICU], gastroenterologists [GI], nurses, and hospital administrators. Participants were chosen from a representative sample of six community or academic-based hospitals across Canada that had taken part in a national Canadian Audit on the management of NVUGIB. The interview questions addressed themes related to specific prioritized NVUGIB guidelines.

**Results:** Participants reported substantive gaps in the implementation of NVUGIB guidelines including (a) substantive lack of knowledge of the specifics of the NVUGIB guidelines (ER, ICU, and nurses), (b) limited belief in the value of guidelines (ER, ICU), (c) limited belief in the value of available tools to support implementation of specific guidelines (GI), (d) lack of knowledge of the roles and responsibilities, as well as limited effective collaboration among respective healthcare professionals in the care of patients with NVUGIB (ER, ICU, GI) (for example, lack of agreement amongst ER, ICU and GI on a definition of "urgent endoscopy"), (f) variability of knowledge and skills of healthcare professionals (for example, nurses' knowledge and skills in endoscopic procedures), and (g) perceived overuse of IV PPI treatment with limited concern regarding cost or side effect implications (all participants).

**Conclusion:** Knowledge, attitude, skill, behavioural, and contextual gaps were found to impact healthcare professionals' adherence to NVUGIB guidelines. In response to these findings a tailored multi-faceted educational and behavioural intervention is being designed, and will be assessed in a national cluster randomized clinical trial.

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#### Dyspeptic Symptoms in an Aspirin (ASA)-Using Population: Celecoxib Versus Naproxen Plus Lansoprazole

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**Purpose:** To evaluate new or existing dyspepsia-like symptoms in patients taking ASA with either celecoxib or naproxen plus lansoprazole.

**Methods:** In a 12-wk prospective, randomized, double-blind trial, prevalence of endoscopic ulcers was evaluated in 1045 subjects taking daily  $\leq 325$  mg ASA and 200 mg celecoxib QD (CEL) or 500 mg naproxen BID with 30 mg lansoprazole QD (NAP/LAN). At baseline and after 4, 8 and 12 wks of treatment, dyspepsia symptoms were assessed using both a 4-point scale [0 (none) to 3 (severe)] and Severity of Dyspepsia Questionnaire (SODA).

**Results:** As previously reported, endoscopically confirmed prevalence of gastroduodenal ulcers was 9.9% CEL (42/426) and 8.9% NAP/LAN (38/428). Baseline mean combined dyspepsia scores (sum of severities for abdominal pain, nausea, vomiting, and heartburn) were similar (CEL 1.8, NAP/LAN 1.7), and the mean increase from baseline was greater in CEL versus NAP/LAN at wks 4 (+0.7 vs +0.3,  $P = 0.012$ ), 8 (+0.7 vs +0.5,  $P = NS$ ) and 12 (+0.8 vs +0.5,  $P = 0.043$ ). Among those with dyspepsia at baseline (212 NAP/LAN, 220 CEL), more subjects reported symptom resolution with NAP/LAN versus CEL at wks 4, 8, and 12 (31 vs. 18%; 33 vs. 15%; and 32 vs. 19%, respectively;  $P \leq 0.003$ ). Among those without dyspepsia at baseline, similar proportions developed new-onset dyspepsia (36–42% CEL, 36–38% NAP/LAN). More subjects treated with NAP/LAN reported improvement in heartburn and belching compared to those treated with CEL at wks 4, 8, and 12 ( $P < 0.05$ ). In the 299 subjects who completed SODA, mean baseline scores were similar between the NAP/LAN and CEL treatment groups (16.3 vs 15.8 pain intensity, 13.9 vs 14.0 nonpain symptoms, 14.1 vs 13.6 satisfaction, respectively). A greater mean improvement from baseline in the nonpain symptoms scales was observed at wks 4 and 8 in NAP/LAN versus CEL (−0.5 vs. +0.4 at wk 4; −0.7 vs. +0.4 at wk 8;  $P \leq 0.025$  for each). There were no other significant differences between NAP/LAN and CEL groups in SODA scores. There was no significant difference in the proportions of subjects who discontinued the study due to GI symptoms (CEL 1.2% vs NAP/LAN 1.3%).

**Conclusion:** While the incidence of new-onset dyspepsia symptoms in both groups of ASA-users was similar, subjects with baseline dyspeptic symptoms improved to a greater extent with NAP/LAN than with CEL.

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#### Novel Biopsy Technique for Diagnosis of Gastric Subepithelial Lesions

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**Purpose:** Adequate diagnosis of the etiology of gastric subepithelial lesions seen on upper endoscopy is challenging secondary to current techniques used to obtain a representative biopsy specimen. Traditional tunnel biopsy has a reported yield of 17% compared to EUS-FNA which has a yield of 80%. In this study we describe a series of patients in which an alteration of the traditional tunnel biopsy technique yields improved rates of diagnosis of the etiology of gastric subepithelial lesions.

**Methods:** Seven consecutive patients with gastric subepithelial lesions seen on routine endoscopy were referred for evaluation. On initial endoscopic ultrasound, none of the subepithelial lesions were cystic or contained blood vessels as confirmed by Doppler ultrasound.

Subsequently, endoscopy was performed on each of the seven subepithelial lesions. Using Cook forceps, five to seven biopsies were taken from the same area of the mucosa in the standard tunnel fashion. Following this, an altered technique was used in which closed biopsy forceps were placed in the previously biopsied area and while applying pressure, the forceps were opened and closed such that the mucosa could be further separated and dissected. After doing this five to seven times, the closed forceps were able to penetrate the mucosal surface and move safely into the lesion. Multiple biopsies were then taken directly from the subepithelial tissue.

**Results:** A diagnosis of the etiology of the gastric subepithelial lesion was obtained in six of the seven cases (86%). The diagnoses included lipoma (2 cases), leiomyoma (2 cases), GIST (1 case), and a pancreatic rest (1 case). In the remaining case, spindle cells were obtained but a leiomyoma or GIST could not be definitively diagnosed. No acute complications including bleeding, perforation or infection were observed in any of the seven patients.

**Conclusion:** An altered technique using standard biopsy forceps to dissect the epithelial mucosal surface followed by direct biopsy of the submucosal tissue yielded an etiology in 86% of the cases studied. In larger case series to date an etiology using standard tunnel biopsy technique was found in only 17% of cases. This technique offers an advantage to EUS-FNA, which yields similar rates of diagnosis of etiology of subepithelial lesions, in that histology can be obtained. Larger case series with a randomized prospective trial would be required to validate the results obtained using this technique in our series as compared to traditional tunnel biopsy and EUS-FNA techniques.

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#### Can Polaprezinc Be Attributed To Reduce the Risk of Gastric Carcinogenesis in *Helicobacter pylori*-Positive Young People?

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**Purpose:** Polaprezinc, an insoluble zinc complex of L-carnosine, was developed for gastric ulcer treatment and reported to inhibit the development of *Helicobacter pylori* (H. pylori) induced gastritis. Metallothionein (MT), which is inducible by dietary zinc (Zn), has been proven to sequester reactive oxygen species and reduce tissue damage. Furthermore, our previous study reported high MT expression in gastric mucosa attenuated H. pylori-induced gastritis and reduced the risk of gastric carcinogenesis.

This study investigates the effect of polaprezinc on H. pylori-induced gastritis and evaluates the relationship with gastric MT levels in young people.

**Methods:** Fifteen H. pylori-positive subjects (HP+, 26.3 ± 3.8 years) and 15 negative subjects (HP-, 25.6 ± 2.4 years) were entered in this study. RT-PCR of MTIIA was performed in antral biopsy samples. Severity of gastritis was evaluated according to the updated Sydney System. The same assessment was repeated after polaprezinc 150 mg b.d. (Zn 33.9 mg included) was received for 4 weeks. Serum Zn was examined in all patients before and after polaprezinc medication.

**Results:** Good compliance was obtained without complications in both groups. Serum Zn was significantly high in both subjects after polaprezinc medication but within the normal range. MT expression was higher in HP- than HP+ and had a negative correlation with severity of gastritis before medication. Four weeks after polaprezinc medication, MT expression in HP+ was significantly recovered but HP- had no significance. The severity of gastritis in HP+ was relatively restored but not significant.

**Conclusion:** Four weeks after polaprezinc medication, MT expression in H. pylori-positive gastric mucosa is recovered and H. pylori-induced gastritis is relatively restored. Polaprezinc may be attributed to reduce the risk of gastric carcinogenesis through the reinforcement of MT expression in young people.

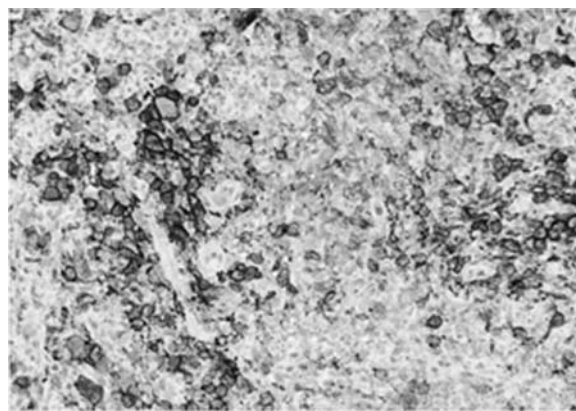
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#### A Patient with Gastric Hodgkin's Lymphoma

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**Purpose:** A 58-year-old black male presented to the hospital with constant abdominal pain. The pain was upper abdominal in location without any radiation, achy in character associated with a 30 lb. weight loss over the prior six months. The patient denied nausea, vomiting, changes in bowel habits, melena or hematochezia. Past medical history was significant for history of Stage III B Hodgkin's Lymphoma diagnosed more than 18 years ago at which time, the patient was treated partially with chemotherapy. He had subsequently refused further treatment.

Physical Examination was significant for a large fixed, non-tender abdominal mass measuring 15 × 10 cm filling the entire abdomen. Rectal examination was negative for blood or melena. Lab evaluation revealed microcytic, hypochromic anemia later characterized to be iron deficient with normal liver tests and renal function. CT abdomen (Fig. 1) showed a large retroperitoneal mass with compression of the stomach and infiltration of the spleen. Upper Endoscopy showed a large friable, ulcerated mass in the fundus. Colonoscopic examination was normal. Histopathological examination showed diffuse infiltration of the tumor cells into the mucosa, submucosa and muscularis propria which stained positive for CD 15 and CD 30 (Fig. 2). A histopathological diagnosis of classical type Hodgkin's Lymphoma was made.



Gastric Lymphomas are relatively uncommon comprising less than 10% of all gastric neoplasms. At least 60% of the gastrointestinal lymphomas arise in the stomach. Non Hodgkin's Lymphomas represent 2–8% of all gastric malignancies. Hodgkin's disease of the stomach, either primary or secondary to

systemic disease is rare. Gastrointestinal involvement by Hodgkin's disease is reported in fewer than 10% of patients with residual Hodgkin's disease at autopsy.[figure1][figure2]

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### Iron Pill Gastropathy: A Case Report and Review of the Literature

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**Purpose:** Despite the widespread use of oral iron supplements, the entity of "iron pill gastritis" has remained largely unrecognized in the Gastroenterology literature. Our patient is an 85 year-old man who presented with a several-month history of melena. Pertinent medications included daily lansoprazole 30 mg and aspirin 81 mg. He had been taking ferrous sulfate 325 mg twice daily for iron deficiency anemia for the prior 8 weeks. History included coronary artery disease, compensated congestive heart failure, and hypertension. The patient had a history of an upper gastrointestinal bleed 2 years prior to this evaluation, secondary to aspirin and celecoxib use. Upper endoscopy revealed a large esophageal ulcer, multiple duodenal ulcers, and no gastric ulcers. Testing for *Helicobacter pylori* was negative. Physical exam revealed stable vital signs and no orthostasis. Examination was normal except for guaiac-positive stool. Hematocrit was stable at 36%. Subsequent upper endoscopy revealed a normal esophagus and multiple sessile diminutive polyps in the gastric fundus. A non-bleeding 4 × 8 mm gastric ulcer with pigmented material was found in the gastric body. Histopathologic evaluation of gastric biopsies obtained from the ulcer revealed foveolar hyperplasia with abundant granular brown pigment, consistent with iron pill gastropathy. The patient was placed on twice daily oral lansoprazole at a dose of 30 mg, and oral iron was discontinued. A follow-up upper endoscopy performed one month later revealed no evidence of active ulceration. The patient has been maintained on lansoprazole 30 mg twice daily and aspirin 81 mg daily. He has experienced no further gastrointestinal problems. Iron injury is thought to result from a direct corrosive action on the gastrointestinal mucosa. A previous study found gastric ulcers in association with oral iron use. Histology of these biopsies showed heavy iron deposition within ulcer granulation tissue, in connective tissue, and in blood vessels of the lamina propria. Ulceration appeared to have preceded the initiation of iron therapy, suggesting that iron use exacerbated a pre-existing condition. Few clinicians are aware that oral iron has been associated with gastropathy that can lead to the development of peptic ulcer disease. Our case provides an illustration of this rare but important entity and highlights the importance of co-morbidity and concomitant use of low dose aspirin.

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### Usefulness of Microvascular Diagnoses of Early Gastric Cancer Using Magnifying Endoscopy

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**Purpose:** In 2001, Yao K et al. reported the characteristics findings for intestinal-type gastric cancer were an irregular microvascular pattern (IMVP), and the presence of a Demarcation Line (DL) using magnifying endoscopy, between the cancerous and non-cancerous mucosa.

The aim of this study was to examine the following two items regarding the usefulness of microvascular diagnoses of intestinal-type gastric cancer. (1) Findings of an index that shows, in a more concrete form, IMVP. (2) Significance of IMVP and DL to serve in the diagnosis of its gastric cancer.

**Methods:** Period was December 2006 through May 2007. Subjects were 17 cases of intestinal-type gastric cancers which showed depressed in shape, while control group consisted of 72 cases of benign erosions. Microvascular patterns were divided into four types: irregularity of vessel arrangements;

vessel caliber disparities; vascular density increases; vessel multibranchings. If any one of these categories applied, then diagnosis of IMVP was made. Gastric cancer diagnostic precision were determined according to sensitivity, specificity, odds ratio (OR), and positive predictive value (ppv).

**Results:** I. All four categories showed high percentages for gastric cancer, with statistically significant differences.

II. The gastric cancer diagnostic precision for each vascular pattern were investigated. As for specificity and ppv, all four categories showed roughly 90% or higher.

As for sensitivity, however, only irregularity of vessel arrangements were as high as 60%.

III. Used as diagnostic precision in gastric cancer, DL sensitivity and specificity were 82% (14/17) and 53% (29/55), while IMVP one were 59% (10/17) and 99% (71/72). DL (+) of ppv for gastric cancer was 26% (14/53), while IMVP (+) of it was 77% (17/22). The DL OR was 4.4 (14×35/3×37), while the IMVP one was 101.7 (10×71/7×1)

**Conclusion:** 1. As an index for grasping IMVP, irregularity of vessel arrangements was useful.

Both the specificity and ppv of it showed high levels of gastric cancer diagnostic precision. Sensitivity, however, was 60%. 2. If we perform a biopsy of depression lesion in which DL is confirmed, we may expect to detect approximately 80% of gastric cancer, but may cause the biopsy of approximately 50% of benign erosion. As for IMVP, while approximately 60% of gastric cancer will be identified, it is surmised that the findings show that benign erosion will be mostly unobserved.

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### Relationship of Symptoms to Quality of Life in Patients with Gastroparesis

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**Purpose:** Understanding symptom severity and the effects of symptoms on quality of life (QOL) in patients with gastroparesis may provide clinicians useful information to help guide treatment. The aim of this study was to identify specific gastrointestinal symptoms that most severely affect QOL in patients with gastroparesis.

**Methods:** New patients with gastroparesis in 2006 were given the Patient Assessment of Upper Gastrointestinal Symptoms (PAGI-SYM) which evaluates symptom presence and severity using a 6-point Likert scale from 0 (none) to 5 (very severe) and the Patient Assessment of Upper Gastrointestinal Disorders-Quality Of Life (PAGI-QOL) questionnaire which covers five domains (daily activity, diet, psychological, clothing, relationship) and associates higher scores with worsening QOL with responses ranging from scale of 0-5. The PAGI-SYM questionnaire is a 20-item tool, which includes the 9 Gastroparesis Cardinal Symptom Index (GCSI) questionnaire.

**Results:** During 2006, 53 new patients with gastroparesis were seen and filled out both questionnaires. The average age was 40 years, 42 patients were female (79%), and 17 patients had diabetic gastroparesis (32%). The GCSI score was 26.3 ± 1.2 and correlated with PAGI-QOL score (r = 0.47). The predominant symptom reported by the patients on the PAGI-SYM questionnaire was nausea (23 pts; 43%) followed by vomiting (13 pts; 25%) and abdominal pain (9 pts; 17%). Patients with vomiting as the predominant symptom had the highest (worse) QOL score (3.28 ± 0.25) when compared to nausea (3.01 ± 0.21, P = 0.41) and abdominal pain (2.99 ± 0.44, P = 0.55). Of the five QOL domains, the psychological QOL domain (3.68 ± 0.32) was highest in patients with vomiting as the predominant symptom, whereas the diet QOL domain was the highest in patients with the predominant symptom of nausea (3.61 ± 0.26) or abdominal pain (3.48 ± 0.32). In these patients with gastroparesis, the QOL questions associated with the worst QOL scores were: 1) Avoided certain types of food (4.13 ± 0.03); 2) Concern about what you can and cannot eat (4.11 ± 0.02); and 3) Frustrated about not being able to do what you wanted to do (4.06 ± 0.03).

**Conclusion:** In patients with gastroparesis, although nausea was the most prevalent predominant symptom, vomiting was associated with the worst



QOL score. Nausea and abdominal pain affected the diet domain, whereas vomiting affected psychological domain the most. Use of the PAGI-SYM and PAGI-QOL questionnaires helps to understand the impact of symptoms on quality of life in patients with gastroparesis.

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### Aspirin Use in the Setting of Acute Myocardial Infarction and Peptic Ulcer Bleeding Does Not Increase the Rebleeding Rate

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**Purpose:** To determine if the use of aspirin or other anti-platelet agents is associated with adverse outcomes in patients with a bleeding peptic ulcer in the setting of acute myocardial infarction.

**Methods:** Patients with a bleeding peptic ulcer and a concurrent acute myocardial infarction were evaluated from 2 tertiary care centers between 1999 and 2007. The pattern of aspirin (ASA) use was determined. Peptic ulcer rebleeding rates and cardiac outcomes were assessed.

**Results:** 102 patients were evaluated retrospectively. Seventy nine patients (78%) received ASA and 46 patients (45%) received clopidogrel during an acute myocardial infarction. 34 patients (33%) were continued on ASA therapy after peptic ulcer bleeding whereas the remaining 68 patients (67%) had ASA held temporarily or discontinued during hospitalization. Patients who had ASA continued were more likely to have had a STEMI, IIb/IIIa inhibitor use, percutaneous coronary intervention and/or CABG ( $P < 0.05$ ). There was no difference in the rebleeding rate from ulcers with low risk stigmata between patients who continued ASA compared to those who had ASA held or discontinued (4.0% vs 7.5%). Among patients with high risk stigmata, there was also no difference in the rebleeding rate (23% vs 29%). When ASA was continued, there was no increase in the rebleeding rate when clopidogrel was used or not (7% vs 11%). Mortality tended to be lower in patients who had ASA continued compared to those who had ASA held or discontinued (9% vs 16%).

**Conclusion:** Aspirin does not appear to increase the rate rebleeding in patients presenting with peptic ulcer bleeding in the setting of an acute myocardial infarction.

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### Implanted Gastric Pacemaker for the Treatment of Diabetic Gastroparesis: A University Hospital Experience

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**Purpose:** Investigate the efficacy of gastric pacemaker implantation in the treatment of diabetic gastroparesis (DGP) in symptom control and quality of life.

**Methods:** Eleven gastric pacemaker implantation surgeries were performed from October 2004 to August 2006 at Medical College of Georgia. Five patients with clearly documented DGP who failed medical management were treated with gastric pacemaker implantation surgery and available for study. Mean age was 39.4 years old. Three of the patients were women. Average duration of symptoms prior to pacemaker implantation was 4.7 years. Patients were followed for an average of 20 months after gastric pacemaker implantation. Several symptom scoring systems including Total Symptom Score (TSS) and Vomiting Frequency Score (VFS) were measured in all patients at baseline and after implantation. Patients were evaluated for subjective signs of illness according to self-reported VFS (range, 0 to 4) and TSS, measuring for nausea, vomiting, bloating, abdominal pain, and anorexia (range, 0 to 24 for severity and frequency each). Complications related to surgery or implanted device and hospitalizations related to gastroparesis were recorded.

Dependence on medications for motility, nausea, and pain were also recorded before and after implantation.

**Results:** All patients except one had significant improvement in symptoms scores following gastric pacemaker implantation. Mean improvement in TSS was 54% for severity and 21% for frequency of symptoms. Total TSS mean improvement was 37%. VFS mean improvement was 61%. Two patients required at least one hospitalization for DGP-related symptoms after implantation. One patient required repeat surgery for pacemaker lead dislodgement. Overall, patients required less antiemetics, motility agents, and pain medication after implantation. No deaths occurred in these five patients.

**Conclusion:** Gastric pacemaker implantation provides clinical improvements in patients with DGP who have failed medical treatment.

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### Gastric Electrical Stimulation for Gastroparesis – The Temple Experience

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**Purpose:** Gastric electric stimulation (GES) is used to treat patients with medically refractory gastroparesis. The aims of this study were: 1) to review our experience with GES for the treatment of refractory gastroparesis; and 2) to determine if there are factors that might favorably impact clinical outcome.

**Methods:** 100 patients with refractory gastroparesis have been treated with Enterra GES (Medtronic, Inc) at our institution over the last 6 years. At follow-up visits, patients were given the Patient Assessment of GI Symptoms (PAGI-SYM) questionnaire and asked to rank their symptoms using a Clinical Global Patient Assessment scale (CGPA) ranging from -7 (a very great deal worse) to +7 (a very great deal better).

**Results:** Of 100 patients implanted, 75 patients still had an active stimulator at the time of this analysis. 8 patients have died; 14 patients had stimulators explanted due to infection (4), gastrectomy (2), lead/pacer erosion (3), MRI (4), shocks (1); and 3 patients had no follow-up. Average follow-up was 318 days (range 34–1473 days). 63 out of 75 patients (84% per protocol; 63% intention to treat) currently receiving GES reported symptomatic improvement, 6 remained the same, and 6 worsened. Average CGPA score of the 75 patients was  $3.2 \pm 0.4$  (SEM), falling in the “somewhat better” category. The 33 patients with diabetic gastroparesis had a higher average CGPA score than the 42 patients in the idiopathic group ( $4.2 \pm 0.5$  vs  $2.4 \pm 0.5$ ;  $P = 0.005$ ). The 61 patients with nausea/vomiting as the primary symptom had a higher CGPA score than the 14 patients with abdominal pain ( $3.4 \pm 0.4$  vs  $2.3 \pm 0.8$ ;  $P = 0.020$ ). The 32 patients using narcotic analgesics regularly had a lower CGPA score than the 43 patients in the non-narcotic group ( $2.3 \pm 0.6$  vs  $3.9 \pm 0.5$ ;  $P = 0.014$ ). Among the diabetics, those with nausea/vomiting as their primary symptom felt more improvement than patients with abdominal pain ( $4.5 \pm 0.5$  vs  $3.3 \pm 0.8$ ;  $P = 0.027$ ). The same trend was present among the idiopathic population ( $2.4 \pm 0.6$  vs  $0.7 \pm 1.2$ ;  $P = 0.034$ ).

**Conclusion:** The majority of patients undergoing gastric electric stimulation stated their symptoms were better than prior to stimulation. Patients with nausea/vomiting as primary presenting symptom responded better than patients with abdominal pain. Diabetic gastroparesis responded better than patients with idiopathic gastroparesis. Importantly, this study has delineated three factors that appear to impact on a favorable clinical response – etiology, predominant symptom, and narcotic use.

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### Ischemic Gastritis; an Unusual Cause of Abdominal Pain and Gastric Ulcers

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**Purpose:** Ischemic gastritis is considered to be an uncommon cause of gastrointestinal symptoms. We are presenting a patient with history of severe

abdominal pain, celiac artery stenosis and endoscopic findings of ischemic gastritis, who had complete resolution of pain and endoscopic findings after celiac artery stenting.

#### Methods: CASE REPORT:

**Results:** Patient was a 70 yrs old white male who presented to the emergency room (ER) with a history of chronic epigastric pain for the last several months. The pain was sharp, moderate in intensity, non-radiated and was associated with nausea. For the last two weeks before coming to ER the pain was more intense and persistent. He reported a 100 Lbs of weight loss for the last five months. Significant past medical history included coronary artery disease, type II diabetes and hypertension. The physical examination revealed a soft, nondistended abdomen with mild tenderness in epigastrium and right upper quadrant. Pertinent laboratory studies included a white blood cells count of 15,000 with 14% bands and an elevated creatinine of 2.4 mg/dl. The CT scan of the abdomen showed wide spread atherosclerosis. An upper endoscopy revealed extensive gastric erythema with large superficial, irregular ulcers through the body and antrum. Biopsies obtained for the gastric ulcers were interpreted as ulcerative gastritis by the pathologist. Because of the endoscopic findings, severe atherosclerosis by abdominal CT and no resolution of symptoms with standard treatment with proton pump inhibitors, patient underwent a magnetic resonance angiogram. The study showed significant stenosis of the celiac trunk with atherosclerotic calcification at origin of celiac axis and superior mesenteric artery. Patient subsequently underwent stenting of the celiac artery. After the stent was placed, the patient had a complete resolution of his abdominal pain. A repeated upper endoscopy performed six weeks later showed almost complete healing of the gastric mucosa.

**Conclusion:** This case represents an unusual cause for abdominal pain and gastric ulceration. The diagnosis of ischemic gastritis should be considered in patient with a vascular disease history and unexplained upper gastrointestinal symptoms.

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##### Comparisons of Alimentary Tract Transit Times among Normal Subjects from Two Multicenter Trials Using SmartPill Wireless pH/Pressure Recording Capsule: Its Clinical Implication

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**Purpose:** The SmartPill (SP) wireless pH/pressure recording capsule was approved for assessment of gastric emptying (GET) based on data from a gastroparesis (GP) trial. In a separate study colonic transit time (CTT) measured by SP in patients with chronic constipation (CC) was similar to CTT measured with Sitzmarks. These trials encompassed not only two separate sets of healthy volunteers, but also two different test meals.

**Aim:** To compare GET, small bowel transit time (SBTT), CTT, and whole gut transit time (WGTT) from CC and GP trials utilizing different test meals. **Methods:** In CC study, 68 (32 F, mean age of 37 y) and in GP trial 50 (22 F, mean age of 35 y) controls were enrolled. While fasting, subjects swallowed the SP with a bar (SmartBar; 260 kcal,) and Sitzmarks capsule in the CC trial; or, with standardized meal (<sup>99</sup>TcEggbeaters, 255 kcal,), in GP study. The WGTT was measured from the time of ingestion of the SP until an abrupt loss of signal. The time from ingestion to rise of pH exceeding pH 4.0 was defined as GET. A sudden drop of 1 pH unit >5 min. was regarded as an ileo-caecal (I-C) arrival. By subtracting GET from I-C time, SBTT and CTT were determined. Based on statistical analysis with Mann-Whitney Test, results are presented as median and 25%-75% range.

**Results:** The median WGTT in both groups was similar (27.1, 22.1–45.5 hrs, vs. 28.0, 23.2–36.8 hrs range;  $P = 0.872$ ). The CTT was also similar (20.7, 15.4–38.1 hrs, vs. 18.4, 13.0–27.7 hrs range;  $P = 0.315$ ). The SBTT

in controls from the CC trial was 25% faster (3.5, 2.8–4.4 hrs range) than GP study (4.7, 3.8–6.2 hrs range;  $P = 0.001$ ). The GET in CC trial was 17% faster (2.9, 2.5–3.8 hrs range) than in GP trial (3.5, 3.0–3.9 hrs range;  $P = 0.045$ ). *Of note:* the mean values for GET, SBTT, CTT, and WGTT in both groups were similar.

**Conclusion:** 1. SP technology represents a new test for assessing TT within all segments of the GI tract. 2. The difference in the median values of GET and SBTT is because the data was not normally distributed in CC trial. 3. Our results provide a reference for normal values for the office use of SP in the future where SmartBar will be the standard meal.

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##### Primary Prevention by Omeprazole 20 mg Daily of the Adverse Gastrointestinal Effects of Short-Term Non-Steroidal Anti-Inflammatory Drug Use in Healthy Subjects: A Randomized, Double-Blind, Placebo-Controlled Study

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**Purpose:** To evaluate in healthy, episodic NSAID users the effectiveness of omeprazole at the U.S. approved OTC dose (20 mg daily) as primary prevention of the adverse gastrointestinal effects of short-term NSAID use. **Methods:** We performed a double-blind, single-site study of generally healthy subjects aged 50–75 who had no specific risk factor for NSAID-related complications, did not take chronic NSAIDs, and had no endoscopic lesions at baseline. Subjects were randomized to a 6.5 day treatment of naproxen (NPX) 500 mg BID plus omeprazole (OMP) 20 mg QD or NPX 500 mg BID plus placebo, after undergoing a baseline endoscopic examination and symptom questionnaire. The primary endpoint was the incidence of gastroduodenal ulceration (GDU) after completion of treatment; secondary endpoints included a change in dyspepsia score [by Severity of Dyspepsia Assessment (SODA)], and the incidence of GDU and/or > 5 erosions. Gastroduodenal biopsies were taken at both endoscopies for future molecular analysis for *H. pylori* (HP) evaluation.

**Results:** A total of 70 subjects were randomized and 66 completed the study. Age, sex, and HP status were similar between the arms. Fewer subjects in the NPX plus OMP group developed GDUs compared to the NPX plus placebo group (11.8% vs. 46.9%,  $RR = .25$ ,  $P = .002$ ). This protective effect of co-prescription of omeprazole was greatest in subjects infected with HP. NPX plus OMP was also associated with a significant decrease in the risk of GDU and/or >5 erosions. By SODA testing, subjects taking NPX plus OMP experienced less dyspepsia than those taking NPX plus placebo. HP was associated with an increased risk of ulcer in the NPX plus placebo group, while dyspeptic symptoms were associated in both groups with endoscopic ulcers.

**Conclusion:** (1) OMP at the U.S. approved OTC dosage of 20 mg daily reduces but does not eliminate gastroduodenal ulcers and dyspeptic symptoms caused by short-term non-selective NSAID use in 50–75 year old intermittent NSAID users; (2) the benefit of co-prescription is greatest in HP-positive individuals; (3) endoscopic injury related to NSAIDs is associated with dyspeptic symptoms, and is increased in HP-positive subjects.

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##### Adjudication of GI Events from Long-Term Placebo-Controlled Trials Provides Evidence for GI Safety and Tolerability of Celecoxib vs Placebo

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**Purpose:** To analyze incidence of clinically significant upper or lower gastrointestinal adverse events (CSULGIEs) of celecoxib vs placebo, using adjudicated gastrointestinal (GI) data from the Adenoma Prevention with Celecoxib (APC), and Prevention of Colorectal Sporadic Adenomatous Polyps (PreSAP) studies.

**Methods:** In APC, 2035 subjects were randomized to celecoxib 200 mg BID, 400 mg BID, or placebo for 3 years. In PreSAP, 1561 subjects were randomized to 400 mg QD or placebo for 3 years. Adverse events (AEs), bleeds, perforations, obstructions or ulcers were evaluated up to 30 days last dose by a blinded GI Endpoint Adjudication Committee (GIEAC). Subjects with GI AEs, GI-related deaths, or Hb fall 3 g from baseline were included. Time between first dose and CSULGIE was analyzed by a Cox proportional hazards model, stratified by study, with aspirin as covariate. Age, gender, clinical history were also analyzed.

**Results:** Of total population reporting AEs (N = 3588), 97 subjects met inclusion criteria and were reviewed by the GIEAC. 54 were adjudicated as having CSULGIEs (1.62% for celecoxib; 1.30% for placebo). Incidence of CSULGIEs was higher among aspirin-users in both groups (2.99% vs 1.17% celecoxib; 2.83% vs 0.81% placebo). No significant difference was shown in hazard ratio (HR) or relative risk (RR) of celecoxib vs placebo. HR of celecoxib vs placebo was 1.24 with upper 0.025 CI at 2.21 (rejects non-inferiority). There were no significant differences in RR of CSULGIEs between treatments in either aspirin (RR 1.06, 95% CI 0.48, 2.34,  $P = 0.894$ ) or non-aspirin users (RR 1.44, 95% CI 0.64, 3.25,  $P = 0.374$ ). Aspirin and age were significant contributors of toxicity.

**Conclusion:** In this pooled analysis, testing for non-inferiority, incidence of CSULGIEs was equivalent for celecoxib and placebo. Importantly, there were few events and the analysis was underpowered. These findings support celecoxib's long-term GI safety and tolerability, and show long-term aspirin use is associated with significant GI toxicity.

	P-value	HR	95% CI
Celecoxib	NS	1.25	0.71–2.23
Aspirin	0.0006	2.63	1.52–4.57
Age (>65 y)	0.0366	1.79	1.04–3.08

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### Effect of *Helicobacter pylori* Infection on Gastric Cancer Development

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**Purpose:** Evaluated the effect of *H. pylori* infection on COX-2, IL-1b, IL-8, Bax, Bcl-2, MGMT and hMLH1 expression in patients with chronic gastritis and gastric cancer.

**Methods:** Gastric biopsies were obtained from two hundred subjects, 155 with chronic gastritis (125 Hp positive and 30 Hp negative) and 45 with gastric cancer. The expression of COX-2, IL-1b, IL-8, Bax, Bcl-2, MGMT and hMLH1 was analyzed using real time RT-PCR, and allelic variants of cagA and vacA were identified by PCR.

**Results:** mRNA expression of pro-inflammatory COX-2, IL-1b and IL-8, cellular turnover Bax and Bcl-2, and DNA repair MGMT and hMLH1 genes were significantly higher in *H. pylori*-infected patients than in uninfected patients. The expression of IL-1b, IL-8, Bax, Bcl-2 and MGMT in gastric adenocarcinoma tissues were not different from those detected in *H. pylori* negative patients. Regarding COX-2, we found that its mRNA levels were higher than in uninfected patients; on the other hand hMLH1 expression was significantly lower. The genotype cagA+/vacAs1 of *H. pylori* is related with both, high degree of inflammation and the higher levels of mRNA expression

of COX-2, IL-1b and IL-8. The ratio Bax to Bcl-2 decreased significantly in gastric adenocarcinoma tissue, which is correspondent with the findings that apoptosis decreases in tumor tissues.

**Conclusion:** Our data showed that *H. pylori* infection up-regulate the expression of pro-inflammatory genes which increases the synthesis of ROS causing DNA damage. The up-regulation of DNA repair enzymes observed in infected patients seems to be a natural response against the increased pre-mutagenic oxidative DNA adducts generated by the bacteria. Regarding the cellular turnover, the bacteria could promote expressions of Bax, Bcl-2 and COX-2, however it might play a different role in carcinogenesis. Initially *H. pylori* could upregulate the expression of proapoptotic genes (Bax), and this effect might be stronger than its upregulatory effect on Bcl-2. During the development of cancer, upregulatory effects of *H. pylori* on antiapoptotic genes (Bcl-2) and on promitogenic genes (COX-2) might counteract the pro-apoptosis effects of Bax. Additionally, we showed a loss of mismatch repair hMLH1 expression in patients with gastric cancer which may easily increase the mutations rate, affecting the carcinogenesis and tumor progression.

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### Does Increased Primary Resistance to Recommended Antibiotics Really Affect *Helicobacter pylori* Eradication?

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**Purpose:** To evaluate the efficacy of two commonly employed treatments for *Helicobacter pylori* infection and the impact of bacterial resistance to antibiotics on eradication rate during a pharmacokinetic study of eradication therapy.

**Methods:** Seventy-nine consecutive *H. pylori*-positive patients were randomly enrolled to receive a 10-day treatment with either lansoprazole 30 mg plus amoxicillin 1 g and clarithromycin 500 mg (all b.i.d., Group A, N = 40); or bismuth subcitrate 125 mg q.i.d. plus tetracycline 500 mg q.i.d. and furazolidone 200 mg b.i.d. (Group B, N = 39). Patients took the first dose of the therapy on days 1, 5 and 10 under supervision at our facility. *H. pylori* status was reassessed at least 60 days following completion of the therapy and bacterial resistance to the antibiotics was investigated.

**Results:** Four patients from group A and 2 patients from group B were lost to follow up. Both treatments resulted in similar *H. pylori* eradication rate: 82.5%–77% (per protocol), 80.5%–73% (intention-to-treat) in Group A and B, respectively (N.S.). Twelve patients in group A were resistant to clarithromycin and in one of them resistance to amoxicillin was also present. In Group B there were only two patients with resistance to tetracycline. No resistance to furazolidone was detected. Pre-treatment resistance did not impact eradication rates for both groups.

**Conclusion:** Primary resistance to clarithromycin or amoxicillin previously considered a potentially serious problem for the eradication of *H. pylori* infection may be not as important as other factors such as compliance for those patients using these drugs.

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### *Helicobacter pylori* Virulence Marker from an Area of High Prevalence with Low Incidence of Gastric Carcinoma

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**Purpose:** *Helicobacter pylori* (*H. pylori*) infection leading to peptic ulcer and gastric carcinoma is more frequent in developing countries. It is acquired at an early age however, frequency of gastric carcinoma (GC) is low. In the present study, we aimed to determine the tissue *H. pylori* virulence marker cagA and vacA alleles and their association with clinical, endoscopic and histological findings.

**Methods:** Two hundred-forty patients with *H. pylori* infection established by both rapid urease test and histology were studied. The symptoms of the patients were recorded and biopsies (antrum and body) were evaluated histologically. The *cagA* and *vacA* allelic status was determined by polymerase chain reaction (PCR). Patients with GC were compared with non-GC.

**Results:** One hundred and fifty-nine (66%) were males. Abdominal pain 175 (73%) and anemia 21 (9%) were the main presenting features. On endoscopy, 169 (70%) had gastritis, 16 (7%) gastric ulcer, 37 (15%) gastric carcinoma and 18 (8%) duodenal ulcer. *CagA* was positive in 125 (52%) while *VacAs1a* was positive in 163 (68%), *VacAs1b* 82 (34%), *VacAm1* 134 (56%) and *VacAm2* 122 (51%). On histology, acute on chronic inflammation was present in 163 (68%) and chronic in 60 (25%). *CagA* was associated with diagnosis of GC 29 (83%)  $P = 0.003$ , inflammation and metaplasia,  $P = 0.01$  and  $P < 0.001$  respectively. *CagA* S1aM1 was positive in 21 (60%)  $P < 0.001$  and *CagA* S1a 23 (66%)  $P = 0.03$  with GC. The *vacA* alleles S1aM1 was positive in 22 (63%)  $P = 0.04$ , S1bM1 in 10 (29%)  $P = 0.01$  with GC.

**Conclusion:** The majority of our patients presenting with abdominal pain had *cagA* positive gastritis. Genotype *CagA* S1aM1 was more frequently associated with GC. Further studies are required to look into the activity of the *cagA* gene to explain the low incidence of gastric carcinoma in our population.

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### T Regulatory Cells Are Abnormal in Gastroparesis (GP)

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**Purpose:** We have previously shown that many patients with the symptoms of gastroparesis demonstrate coagulation abnormalities associated with autoimmune markers, even in the absence of known autoimmune disease. Many autoimmune conditions have associated immunoregulatory dysfunctions that precede clinical manifestations, but, no controlled studies of cytokines exist in GP.

**Methods:** To investigate the hypothesis that GP patients can have unsuspected underlying immunoregulatory abnormalities, we quantitated T regulatory cells in peripheral blood mononuclear cells (PBMC) from nine symptomatic GP patients (2 m 7 f mean age 44 years) due to DM (N = 2), post-surgical (N = 1), or idiopathic disease (N = 6) and compared the results to 25 normal controls. T regulatory 1 (TR1), TH3 cells and TH1/TH2 ratios were quantitated in PBMC from patients with GP and normal controls by flow cytometry. TR1 cells were defined as CD4+CD25+FoxP3+IL-10+ while TH3 cells were defined as CD4+TGFb+. TH1/TH2 ratios were calculated from TH1(CD4+IFNg+) and TH2 (CD4+IL-4+) values. Results were compared by t-test and reported as mean and 95% CI.

**Results:** TR1 and TH3 cell numbers were both lower in patients with GP. TH1/TH2 ratio was decreased in GP versus normal controls, (See table of results).

**Conclusion:** GP patients have multiple T regulatory cell abnormalities, similar to those seen in various allergic and autoimmune disorders. Both TR1 and TH3 were lower in GP compared to control. An altered TH1/TH2 ratio (favoring TH2 predominance) response was also observed in GP patients, consistent with an established immune imbalance. Further studies of T regulatory cells in GP seem warranted, and may offer help in understanding the mechanisms of other reported inflammatory abnormalities often seen in GP.

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### Multiplex PCR To Detect *H. pylori* in MALToma and Its Role in Treatment and Prognosis: A Case Series

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Cytokine	Control	95% Conf	GP	95% Conf	P
CD4+/CD25++ IL-10 (TR1)	7.41	6.4-8.4	4.18	2.6-5.8	0.0014
CD4+ TGFb (TH3)	0.94	0.8-1.1	0.63	0.4-0.9	0.051
CD4+ IFNg/IL-4	0.87	0.6-1.1	0.33	0.1-0.7	0.0205

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**Purpose:** Gastric mucosa-associated lymphoid tissue (MALT) lymphoma develops in *Helicobacter pylori*-associated chronic gastritis. Current diagnostic techniques for *H. pylori* associated MALToma include CLO rapid urease test, conventional PCR, histologic studies. However, these methods are not very sensitive and do not provide accurate treatment guidance or prognosis. To report a case series in which Multiplex PCR (MPCR) was applied to detect *H. pylori* related MALToma and its use to guide treatment and prognosis.

**Methods:** We performed MPCR in patients with a diagnosis of MALToma. Patients were treated and followed till their MPCR reaction became negative.

**Results:** Four patients with a diagnosis of MALToma demonstrated MPCR positive reactions with negative or positive CLO, culture and pathology for *H. pylori*. In 2 patients, a negative MPCR reaction was used to determine a treatment endpoint. In one patient, in spite of multiple treatment tissue was negative for MPCR but positive for MALToma and it was therefore determined that it might be due to evolved MALToma. In another patient, the MALToma recurred after 9 months in spite of persisted negative MPCR. These two patients with MALToma in spite of negative MPCR received radiation and the MALToma was cured. (Table)

**Conclusion:** In all patients we noted that MPCR was very sensitive and specific for diagnosis of *H. pylori* related MALToma. In all patients, MPCR was utilized to determine treatment efficacy and prognosis.

Patients	EGD	After 2 weeks of Prevpac/ EGD	Repeat 2 weeks of Prevpac/ EGD	Recurrence
Patient 1	+ve MALToma, +ve CLO, +ve H. pylori, +ve MPCR	+ve MALToma, -ve CLO, -ve H. pylori, +ve MPCR	-ve MALToma, -ve MPCR	NO
Patient 2	+ve MALToma, -ve CLO, -ve H. pylori, +ve MPCR	+ve MALToma, -ve CLO, -ve H. pylori, +ve MPCR	-ve MALToma, -ve MPCR (Plus Flagyl)	Yes after 9 Months. Treated with radiation, MALToma resolved
Patient 3	+ve MALToma, -ve CLO, -ve H. pylori, +ve MPCR	-ve MALToma, +ve MPCR	-ve MALToma, -ve MPCR	NO
Patient 4	+ve MALToma, -ve CLO, +ve H. pylori, +ve MPCR	+ve MALToma, -ve MPCR	+ve MALToma, -ve MPCR	?? Evolved MALToma. Treated with radiation, MALToma resolved

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**Helicobacter pylori (Hp) Seropositivity in Patients with Both Negative Rapid Urease Test (CLO) and No Histopathological Evidence of Hp**  
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**Purpose:** Gastric biopsies are obtained routinely during EGD for CLO and histology. However, questions have been raised about a decreased diagnostic

yield of CLO and histology in detecting this organism compared to the original published reports for several reasons, including a gradual decrease in *Hp* infection over the past decade and increase in the use of acid-reducing medications. The aim of the study was to investigate the role of *Hp* serology in patients with negative CLO and no histological evidence of *Hp*.

**Methods:** A total of 776 consecutive patients (age 18–95) who underwent a CLO test at a large tertiary care center in the Midwest between July 2005 to December 2006 were identified. Fifteen patients were excluded due to lack of CLO test verification and 5 due to lack of availability of EGD report. We reviewed the CLO results, EGD reports, available histology (routine hematoxylin-eosin and/or thiazine stain), and aspirin and other NSAID use. Available serology was then compared to CLO and histology in the detection of *Hp* in patients with and without ulcers and erosions detected on EGD. The results were analyzed with the binomial distribution using serology test specificity of 92% provided by the manufacturer (Meridian).

**Results:** A total of 756 patients were studied: 441 (58.3%) males and 315 (41.7%) females (mean age: males, 59.86 years and females, 61.93 years). Most patients were Caucasian (N = 669; 88.5%) with more outpatients (N = 411; 54.4%) than inpatients (N = 345; 45.6%). CLO was positive in 52 (6.88%) patients and negative in 704 (93.12%) patients. *Hp* serology was available in 91 patients of which 16 had it done more than 1 year prior to CLO. In the remaining 75 patients, no gastric biopsies were done on 25 patients. Of these 50, 49 patients had negative CLO and histopathology but 9 (18.4%) had positive *Hp* serology. Exclusion of patients with *Hp* serology done more than 4 weeks before or after the CLO identified 26 patients of which 6 had positive *Hp* serology with this proportion (6/26) being significant, greater than the false positive rate ( $P < 0.05$ ).

**Conclusion:** CLO is positive in a small percentage of patients undergoing EGD. Negative CLO and histology may not be sufficient to exclude infection with *Hp*. Prospective studies assessing the role of *Hp* stool antigen testing and PCR for *Hp*16S ribosomal DNA on gastric tissue are warranted in this patient population.

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### The Role of Flow Cytometry in the Diagnosis and Surveillance of Gastrointestinal Lymphomas

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**Purpose:** We evaluate the accuracy of flow cytometry (FCM) using endoscopic biopsies in the diagnosis and surveillance of GI lymphomas.

**Methods:** We retrospectively analyzed 105 consecutive FCM results on 69 patients with suspicious GI lesions over 11-year period (1996–2007). Eighteen tests (9 patients) were discarded due to inadequate cells for FCM. Of the adequate specimens, 60 were initial-observation samples and 27 were follow-up. FCM was compared to the combined group of H&E and IHC morphology.

**Results:** Male:female ratio was 1:1, mean age 64.5 years (34–83) and mean follow-up period 12.1 months (1–96). There were 54 gastric, 21 small bowel, 11 large bowel and 1 liver samples. All were obtained by cold biopsy forceps except for 3 fine-needle aspirations. Lymphomas diagnosed included 17 MALT, 11 diffuse large B-cell, six follicular, three mantle cell and one T-cell.

Overall, FCM alone compared to H&E and IHC showed sensitivity 91.4%: 95% CI [75.8%, 97.8%], specificity 90.4%: 95% CI [78.2%, 96.4%], positive predictive value 86.5%: 95% CI [70.4%, 94.9%] and negative predictive value 94.0%: 95% CI [82.5%, 98.4%].

Initial FCM results in 60 patients were 21 true positive, 35 true negative, 2 false positive and 2 false negative. One “false positive” had recurrent disease a year later. Both false negatives had definite disease on further follow-up. Analysis showed sensitivity 91.3%: 95% CI [70.5%, 98.5%], specificity 94.6%: 95% CI [80.5%, 99.1%], positive predictive value 91.3%: 95% CI [70.5%, 98.5%] and negative predictive value 94.6%: 95% CI [80.5%, 99.1%].

Following therapy, 27 FCM results were 11 true positive, 12 true negative, 3 false positive, and 1 false negative. Two “false positives” had recurrent disease in surveillance (follow-up period: 1–6 months). Analysis showed sensitivity 91.7%: 95% CI [59.8%, 99.6%], specificity 80.0%: 95% CI [51.4%, 94.7%], positive predictive value 78.6%: 95% CI [48.8%, 94.3%] and negative predictive value 92.3%: 95% CI [62.1%, 99.6%].

**Conclusion:** Flow cytometry is a highly accurate, affordable, quick and widely available test for detecting lymphomas in GI endoscopic biopsies. FCM can be routinely performed as a complementary test to H&E and IHC. For a few discordant cases in which histology and FCM differ, possible explanations are small number of biopsies, difficulty in correctly identifying the involved sites, especially after therapy, and the elusive, complex nature of lymphomas in general.

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### Drug Utilization Review of Acid Suppressants for Bleeding and Other Indications (Durable) – An Audit To Assess the Utilization of Proton Pump Inhibitors and Histamine H<sub>2</sub>-Receptor Antagonists in Canadian Hospitals

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**Purpose:** Inappropriate utilization of proton pump inhibitors (PPI) and H<sub>2</sub>-receptor antagonists (H<sub>2</sub>RA) in inpatients is prevalent, but not well defined due to a lack of standardized grading system of appropriateness. We undertook a national audit to better characterize this situation.

**Methods:** For in-patients receiving a PPI or H<sub>2</sub>RA, demographic, clinical, laboratory, endoscopic, and pharmacological data were collected. Drug regimens were reviewed by experts using standardized adjudication rules. Regimens included intravenous high dose continuous infusion PPI (IVci = bolus followed by ci), bolus IV PPI (IVb), oral PPI, and IV or oral H<sub>2</sub>RA, and were categorized as Endorsed (with dosing accuracy) or not recommended (based on published guidelines), indeterminate (based on other publications), or not recognized.

**Results:** Over 6 months, 1829 patients (age: 63.8 ± 16.9 yrs, 43% female) were included from 12 institutions (6 academic and 6 community settings) in 8 provinces. 28% were taking a PPI and 7% an H<sub>2</sub>RA prior to admission. Mean length of stay was 15.3 ± 18.7 days. The top indication for PPI or H<sub>2</sub>RA use was upper GI bleeding (UGIB) in 28.7%, of which 48% started while in-hospital and 29% did not undergo endoscopy; the remainder did within 41.4 ± 58.8 hrs of symptoms onset. Peptic ulcer was seen in 56.6% (23% with high-risk stigmata).

**Conclusion:** Non endorsed use is noted in 48.3% Ivci, 36.6% Ivb, and 9.5% PO PPI/H<sub>2</sub>RA, while correct dosing is common for endorsed indications (98.6% Ivci, 85.3% Ivb, and 75.0% PO). These data will help design appropriate educational and behavioural interventions to optimize in-hospital prescribing of acid suppressants.

Research supported by AstraZeneca Canada Inc.

Categorization of both PPI and H<sub>2</sub>RA Use

	Endorsed		Indeterminate % [CI]	Not	Not	N
	% [CI]	% correct dosing		Recommended % [CI]	Recognized % [CI]	
IVci	48.3 [40.4, 56.3]	98.6	1.4 [0.4, 4.8]	48.3 [40.4, 56.4]	2.0 [0.7, 5.8]	147
IVci	38.4 [33.4, 43.7]	85.3	17.9 [14.1, 22.3]	36.6 [31.6, 41.9]	7.1 [4.8, 10.4]	336
PO	46.3 [39.4, 53.2]	75.0	30.3 [24.4, 37.0], 61	9.5 [6.1, 14.3]	13.9 [9.8, 19.4]	201

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### Do Minorities Have a Worse Outcome from Primary Gastric Cancer Than Whites?

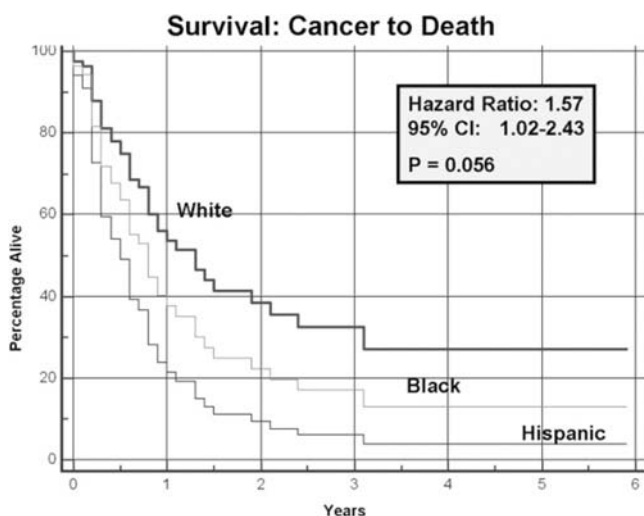
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**Purpose:** The purpose of this study is to compare the gastric cancer survival rates of Blacks, Hispanics, and Whites; and to identify factors that may account for any differences.

**Methods:** The records of all patients with histological documentation of primary gastric adenocarcinoma at a single university medical center from January 2002 through December 2005 were reviewed. Various characteristics were recorded. The predictor variables on ethnicity included sex, age at diagnosis, treatment (with surgery, chemotherapy, or radiation), and cancer stage.

**Results:** During the four year period from January 2002 through December 2005, 76 patients were diagnosed with primary gastric adenocarcinoma. Hispanics developed adenocarcinoma at a younger age than Blacks and Whites (mean age of 61.7 years versus 63.3 and 72.9 respectively). Hispanics and Blacks had significantly more advanced cancer than Whites, as defined by Stage III or IV disease (68.8% versus 39.2% with a difference of 29.6% and 95% confidence interval of 3.24 to 55.96). Hispanics also had shorter mean survival (0.58 years) than Blacks (1.05 years) and Whites (1.08 years). The Cox Proportional Hazards Regression (figure) demonstrated the statistically significant decrease in Hispanic survival, without significant influence of the predictor variables (hazard ratio = 1.57 with 95% confidence interval of 1.02–2.43).

**Conclusion:** Compared to Whites, gastric adenocarcinoma in Hispanics is more advanced, has worse survival, and develops at a younger age; causes for these differences are unknown, but warrant further investigation.[figure1]



### PANCREATIC/BILIARY

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### Clinical Outcomes, Survival Benefits, and Long-Term Stent Patency in Patients with Malignant Biliary Obstruction: A Systematic Review and Meta-Analysis

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**Purpose:** Endoscopic biliary drainage for malignant obstructive jaundice is a viable and popular alternative, but its exact role and the clinical outcomes

of the various available stents are subject to debate. The objective of this study was to review the literature with regard to the clinical outcomes, patency rates, and quality of life in patients requiring endoscopic palliation for malignant obstructive jaundice.

**Methods:** Using PubMed, Medline, Embase, Current Contents, and the Cochrane Database of Systematic Reviews databases (OVID), a literature search was performed for papers published from January 1990 to December 2006. All retrieved papers comparing plastic with metallic stents for palliative biliary decompression, were rated according to the strength of evidence and carefully analyzed.

**Results:** A total of 566 patients were included in our analysis. 273 (48%) patients had plastic stents, and 293 (52%) had metallic stents. In the plastic stent group 144 patients (53%) were males, and 129 (47%) were females. In the metallic stent group 155 patients (53%) were males and 138 (47%) were females. The age of the patients was 21–96 years, with a median age of 72.50 years. The median age for the plastic stent group was 73.01 years (36–96), and that of the metallic stent group was 72.09 years (21–94), which was not statistically significant ( $P = 0.84$ ).

Based on our meta-analysis, the median time of stent patency was 187.7 days for the metal stents, and 95.1 days for the plastic stents, which is statistically significant ( $P < 0.002$ ). While the quality of life was better for all of the patients undergoing palliative endoscopic drainage, there was no evidence of a difference in the technical or therapeutic success, or complication rates between the two groups. However, the median patient survival was also statically higher ( $P < 0.001$ ) in the metal stents group than the plastic stents group (243 days vs. 190 days).

**Conclusion:** Palliative endoscopic drainage affords improved quality of life. With better patency rate and improved patient survival, clinicians should consider using a metal stent as first preference, when there is no other contraindication, in the management of malignant biliary strictures.

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### Clinical Outcomes, and Long-Term Stent Patency in Patients with Malignant Biliary Obstruction: A Systematic Review and Meta-Analysis

Faisal A. Bukeirat, MD\*, Rubayat Rahman, MD. *Digestive Diseases, WVU School of Medicine, Morgantown, WV.*

**Purpose:** Endoscopic biliary drainage for malignant obstructive jaundice is a viable alternative, but its exact role and the clinical outcomes of the various available stents are subject to debate. The objective of this study was to review the literature with regard to the clinical outcomes, patency rates, and quality of life in patients requiring endoscopic palliation for malignant obstructive jaundice.

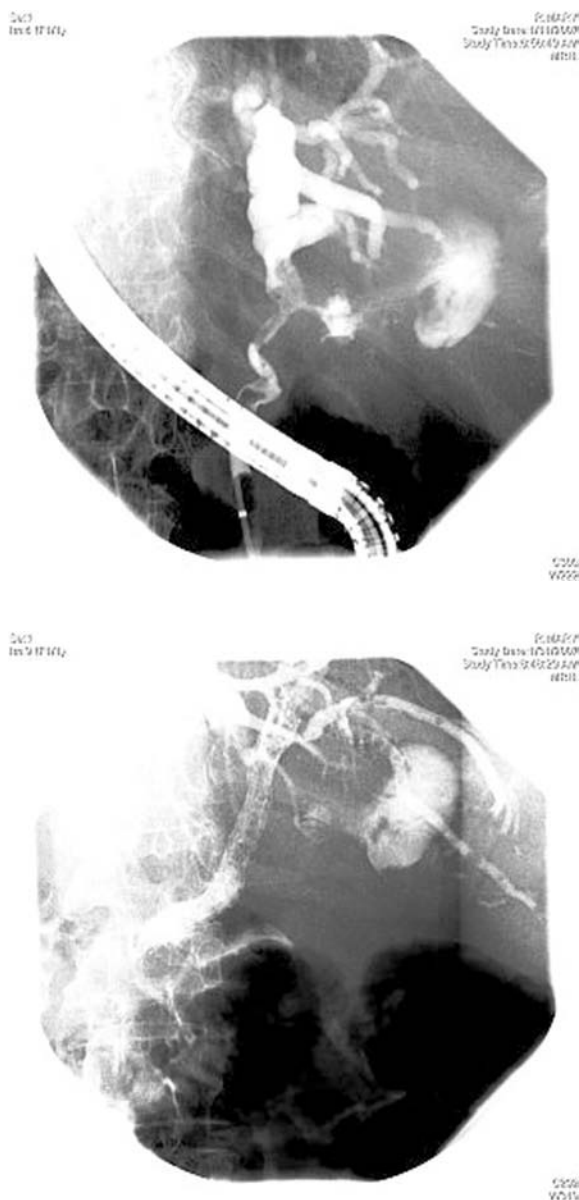
**Methods:** Using PubMed, Medline, Embase, Current Contents, and the Cochrane Database of Systematic Reviews databases, a literature search was performed for papers published from January 1990 to December 2006. All retrieved papers comparing plastic with metallic stents for palliative biliary decompression, were rated according to the strength of evidence and analyzed.

**Results:** A total of 566 patients were included in our analysis. 273 (48%) patients had plastic stents, and 293 (52%) had metallic stents. The age of the patients was 21–96 years, with a median age of 72.50 years. The median age for the plastic stent group was 73.01 years (36–96), and that of the metallic stent group was 72.09 years (21–94), which was not statistically significant ( $P = 0.84$ ).

The median time of stent patency was 187.7 days for the metal stents, and 95.1 days for the plastic stents, ( $P < 0.002$ ). While the quality of life was better for all of the patients undergoing palliative endoscopic drainage, there was no evidence of a difference in the technical success, or complication rates between the two groups. However, the median patient survival was statically higher ( $P < 0.001$ ) in the metal stents group than the plastic stents group (243 vs. 190 days).

**Conclusion:** Palliative endoscopic drainage affords improved quality of life. With better patency rate and improved survival, clinicians should consider

using a metal stent as the preferred option in the management of malignant biliary strictures.[figure1][figure2]



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#### Prognostic Factors in Patients with Advanced Cholangiocarcinoma: Role of Surgery, Chemotherapy, and Body Mass Index

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**Purpose:** Cholangiocarcinoma is an infrequent malignancy that involves the biliary epithelium. It has a poor prognosis with a survival of less than 5% at five years. Radical surgery is the only potentially curative treatment modality, while the impact of chemotherapy on survival remains controversial. Due to the small number of patients, determinants of prognosis in cholangiocarcinoma are not well characterized.

The purpose of this report is to study the factors that may affect survival of cholangiocarcinoma in Lebanon.

**Methods:** A retrospective review of the medical records of 55 patients diagnosed with cholangiocarcinoma at the American University of Beirut between 1990 and 2005 was conducted. Univariate and multivariate analysis were performed to determine the impact of surgery, chemotherapy, body mass index, bilirubin level and other factors on survival.

**Results:** The median survival of all patients was 8.57 months (0.03–105.2). Univariate analysis showed that low bilirubin level (<10 mg/dl), radical surgery and chemotherapy administration were significantly associated with better survival ( $P = 0.012$ ,  $0.038$  and  $0.038$ , respectively). In subgroup analysis on patients who had no surgery, chemotherapy administration prolonged median survival significantly (17.0 vs. 3.5 months;  $P = 0.001$ ).

Multivariate analysis identified only low bilirubin level < 10 mg/dl and chemotherapy administration as independent predictors of associated with better survival ( $P < 0.05$ ).

**Conclusion:** Our data show a significant positive impact of both palliative and postoperative chemotherapy and a bilirubin level <10 mg/dl at presentation on survival in patients with cholangiocarcinoma.

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#### Enteral Self-Expanding Metallic Stent (SEMS) for Palliation of Jaundice in Pancreatic Intraductal Papillary Mucinous Neoplasm (IPMN)

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**Purpose:** There has been one previous report of enteral SEMS placement in the bile duct (BD) for choledochal cyst with cholangiocarcinoma. We report a case of IPMN of the pancreas requiring enteral SEMS.

**Methods:** A 79 yo male was followed for presumed chronic pancreatitis with dilated PD when he developed jaundice. ERCP 12/05 revealed IPMN. Sphincterotomy was done, and a 10 fr plastic stent was placed with improvement. In 10/06 the pt. developed recurrent jaundice and cholangitis. A 10 mm biliary SEMS was placed. After 1 week the pt. returned with cholangitis and no improvement in jaundice. The SEMS had migrated almost completely into the duodenum. It was removed endoscopically and the BD was swept with an 18 mm balloon to remove mucin. Symptoms and jaundice persisted. 2 weeks later a 22 mm diameter enteral SEMS was placed.

**Results:** Patient had persistent relief of symptoms and normalization of bilirubin after placement of enteral SEMS in the BD.

**Conclusion:** 22 mm enteral SEMS can provide effective palliation of jaundice and cholangitis in IPMN when obstruction is due to mucin production and not ductal narrowing.

Table 1. Effect of 22 mm SEMS

	ERCP 1	ERCP 2	ERCP 3	POST 22MM SEMS
TOTAL BILI	9.6	6.9	14.4	0.9
ALK PHOS	901	1055	788	350
ALT	230	182	188	48
GGT	730		428	265
CA 19-9	10			117

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## ABSTRACT WITHDRAWN

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**Detection of Patients at Increased Risk of Pancreatic Cancer Utilizing Electronic Databases**

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**Purpose:** Pancreatic cancer is the four and fifth most common cancer in men and women respectively and has the lowest five-year survival rate of any cancer. Surgical resection offers the only hope for cure; however 52% of patients have stage IV disease at the time of diagnosis. The current problem is there are no means to identify patients who are at risk of developing pancreatic cancer at an early resectable stage. We hypothesize that there may be certain risk factors which predispose patients for pancreatic cancer. If a combination of these factors could be determined then screening exams could be offered to these patients with endoscopic ultrasonography.

**Methods:** A retrospective review of our tumor registry was used to identify 638 patients with pancreatic cancer diagnosed between the years of 1995–2005. Patients that were referred from an outside institution or not routinely followed at Scott & White were excluded. The remaining 397 patients had their electronic medical records reviewed to determine if the incidence of certain factors or combination of factors portend a higher risk of pancreatic cancer. The factors reviewed included: the presence of an elevated amylase or lipase, new onset diabetes, chronic pancreatitis, family history of pancreatic cancer, history of unintentional weight loss, and abnormal pancreatic radiographic imaging. In addition, we also reviewed the same criteria of age/sex matched controls seen at the GI clinic during this same period.

**Results:** Multiple factors on univariate analysis including elevated amylase and lipase, family history of pancreatic cancer, alcohol use, elevated CEA, new onset diabetes as well as use of diabetic medications are present more commonly in patients with pancreatic cancer as compared to their age/sex

matched controls. Multivariate analysis revealed family history of pancreatitis, use of diabetic medications, and history of weight loss or abdominal pain were significantly increased in pancreatic cancer patients versus controls.

**Conclusion:** Conclusions: Our results indicate a combination of the above factors are more common in patients with pancreatic cancer. Patients with these risk factors should be identified while asymptomatic and offered a screening exam, either with CT scan or endoscopic ultrasound depending on local expertise, to find potentially resectable pancreatic cancers.

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**Dissociation in the Sensitivity of Magnetic Resonance Cholangiopancreatography in the Diagnosis of Biliary and Pancreatic Diseases**

Emad Qayed, MD, Qiang Cai, MD, FACC\*. Department of Medicine Division of Digestive Diseases, Emory University School of Medicine, Atlanta, GA.

**Purpose:** Magnetic resonance cholangiopancreatography (MRCP) and endoscopic retrograde cholangiopancreatography (ERCP) are the two currently available important tools in the diagnosis of pancreatobiliary diseases. The aim of this study was to examine the sensitivity of MRCP in the diagnosis of pancreatobiliary diseases using ERCP as the gold standard.

**Methods:** We studied all patients who had ERCP and also MRCP at Emory University Hospital from January 1st 2002 to January 20th 2007. Those who had MRCP beyond 3 months of ERCP, who had liver transplant or biliary surgery between those two tests, and who had incomplete or suboptimal ERCP or MRCP were excluded from the study. We compared the diagnosis suggested by those two tests in eligible patients.

**Results:** 184 patients met the enrollment criteria during the study period. Of those, 136 had abnormalities mainly in the biliary system, and 48 had abnormalities mainly in the pancreas in ERCP. In the 136 patients who had biliary abnormalities, MRCP had the correct diagnosis as ERCP in 111 patients (82% of 136) and incorrect diagnosis in 25 patients (18% of 136). In contrast, in the 48 patients who had pancreatic abnormalities, MRCP had the correct diagnosis as ERCP in 46 patients (96% of 48) and incorrect diagnosis in 2 patients (4% of 48). The dissociation of the sensitivity of MRCP in diagnosis of the biliary diseases and the pancreatic diseases is statistically significant ( $P < 0.05$ ).

**Conclusion:** In this retrospective study, MRCP had more accuracy in the diagnosis of pancreatic diseases than that of biliary diseases when ERCP was used as the gold standard.

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**Retrospective Comparison of Magnetic Resonance Cholangiopancreatography (MRCP) with Endoscopic Retrograde Cholangiopancreatography (ERCP) in the Diagnosis of Pancreaticobiliary Diseases**

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**Purpose:** Magnetic resonance cholangiopancreatography (MRCP) is an alternative to diagnostic endoscopic retrograde cholangiopancreatography (ERCP) for imaging the biliary tree and investigating pancreaticobiliary diseases. The aim of the study is to compare the accuracy of MRCP to that of ERCP in the diagnosis of various obstructive and nonobstructive pancreaticobiliary diseases.

**Methods:** A retrospective analysis was conducted at Emory University Hospital of all patients who underwent ERCP procedures between January 1st 2002 and January 20th 2007. To create a comparison, we looked for MRCPs performed within three months of the ERCP. We excluded patients who had liver transplant or biliary surgery between the two tests, and who had



incomplete or suboptimal ERCP or MRCP. Comparison was made between the final diagnosis suggested by each test. Subanalysis was done to investigate the diseases that caused most inaccuracies in MRCP.

**Results:** Of all patients who had an ERCP performed during this five-year period, 184 patients met the inclusion criteria of the study. Of those 184 patients, 99 (54%) were males and 85 (46%) were females. Average patient age was 55 years.

The MRCP diagnosis agreed with the ERCP in 85.3% of cases (157/184) and disagreed in 14.7% of cases (27/184). Of all comparisons in which MRCP disagreed with ERCP, 48% were related to choledocholithiasis (13/27), 22% to biliary strictures (6/27), 15% to biliary tree anomalies (4/27) and 7% to biliary malignancies (2/27). There were two cases of chronic pancreatitis and ampullary abnormality that were misdiagnosed by MRCP (2/27, 8%).

**Conclusion:** In general, MRCP appears to be a relatively accurate tool to investigate and diagnose pancreaticobiliary disorders. It provided similar results to ERCP in 85.3% of cases. Inaccuracies in MRCP were most commonly related to choledocholithiasis, although a separate study is suggested to evaluate the sensitivity and specificity of MRCP in detecting choledocholithiasis in our patient population.

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### Multiple Biliary Stenting – An In Vitro Comparison Using a Novel ERCP Mechanical Simulator

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**Purpose:** There is a paucity of methods for objective evaluation of ERCP accessories. In this study, we tested the hypothesis that practice on a mechanical simulator allows comparison of performance of different ERCP accessories.

**Methods:** Endoscopists at various level of ERCP experience participated in Hands-on ERCP practice workshops using a mechanical simulator. Accessories for biliary stenting with (Fusion OASIS, Cook Endoscopy) and without (RX, Boston Scientific) the capability of intraductal release (IDR) of the guide wire were compared. Total time taken to insert single or multiple stents across an artificial bile duct stricture using the ERCP simulator and simulated fluoroscopy time were recorded.

**Results:** There was no significant difference in the time required for placement of single stent (Table 1). The accessories that permitted IDR and exchange of guide wire required significantly shorter time to complete placement of three stents (Table 2), most likely because of the absence of need for re-cannulation.

**Conclusion:** Objective comparison of the function of different ERCP accessories is made possible by referencing the time taken to complete a specific task, e.g. single or multiple stenting. The mechanical simulator permits performance of different accessories by the same group of operators to be objectively evaluated. How the results of in vitro practice and comparison using the mechanical simulator will translate in clinical settings remain to be established.

#### Comparison of Single Stenting with 2 Short Wire Systems

IDR	N	Cannulation	Balloon Dilation	Cytology	Stent Insertion	Total Time	SFT
Yes	19	1.5 ± 0.2	2.0 ± 0.2	1.5 ± 0.1	2.2 ± 0.3	8.9 ± 0.6	2.6 ± 0.3
No	21	1.8 ± 0.2	1.6 ± 0.1	1.6 ± 0.2	1.5 ± 0.2*	8.7 ± 0.7	2.2 ± 0.4

Time in minutes (mean ± SEM), IDR = intraductal release, SFT = Simulated fluoroscopy time, \*versus Fusion OASIS,  $P < 0.05$ , unpaired t test

#### Comparison of Time Taken for Triple Stenting

IDR	N	Total Time	Down Time	Recannulation Time	SFT
Yes	9	15.8 ± 1.2	3.5 ± 0.6	0	3.8 ± 0.5
No	9	20.9 ± 1.2*	5.1 ± 1.4	4.6 ± 0.9*	4.2 ± 0.5

Time in minutes (mean ± SEM), \* versus Fusion OASIS,  $P < 0.05$ , unpaired t test

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### Correlation between MRCP and ERCP Findings in Patients Undergoing an ERCP at a Tertiary Care Hospital

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**Purpose:** The sensitivity and specificity of endoscopic retrograde cholangiopancreatography (ERCP) and magnetic resonance cholangiopancreatography (MRCP) have been studied separately. It is very common in the clinical practice to obtain a MRCP followed by an ERCP. To date, there has been no study to correlate the findings between these two studies. Aim: Examine patient characteristics, and outcomes between the MRCP and ERCP findings in patients in a tertiary care hospital.

**Methods:** This retrospective study was undertaken after obtaining appropriate IRB exemption. Patients who underwent MRCP followed by an ERCP in West Virginia University between July 1, 2004 and June 30, 2006 were identified. Patient's demographic information, pre-imaging and pre-procedure relevant laboratory values and diagnostic study outcomes were collected. Data was entered into MS Access and SAS 10.0 was utilized to analyze the data. Two tail  $P$ -value of 0.05 was considered statistically significant.

**Results:** A total of 165 patients were identified who underwent a MRCP followed by an ERCP in West Virginia University Hospital from July 1, 2004 to June 30, 2006. 98 (59%) of these patients were female and 67 (41%) were male. Baseline demographic characteristics were comparable between male and female patients. MRCP over diagnosed ductal dilatation significantly more as compared to ERCP (ERCP 116/165 and MRCP 138/165,  $P < 0.04$ ). Similarly, MRCP also over diagnose the presence of a hepatobiliary mass compared to ERCP (78/165 compared to 61/165,  $P < 0.01$ ). In contrast, MRCP under diagnosed bile duct stones (44/165 for MRCP and 59/165 for ERCP,  $P < 0.01$ ). Similarly, MRCP also under diagnosed both biliary stricture and obstruction a significant percentage of the time (15% and 18% respectively,  $P < 0.05$  for both).

**Conclusion:** In patients presenting with symptoms, signs and laboratory studies suggestive of hepatobiliary pathology MRCP appears to be a less sensitive and specific modality than ERCP for ductal dilatation, mass, stones or obstruction. Thus, ERCP remains the gold standard test for visualization of the hepatobiliary tree.

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### Incidental Bile Duct Stones Diagnosed by EUS

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**Purpose:** EUS of the common bile duct is the most accurate minimally invasive procedure to diagnose choledocholithiasis with accuracy of more than 90%. The true incidence of asymptomatic common bile duct (CBD) stones in patients undergoing EUS examination for unrelated indications is unknown.

**Methods:** We have retrospectively reviewed our initial, single center EUS database for any cases of incidental CBD stones.

**Results:** Two out of 50 EUS procedures (4%) found asymptomatic CBD stones. We describe in details both cases of incidental choledocholithiasis, found on EUS done for unrelated indication.

**Conclusion:** Once an EUS study is indicated, we recommend a complete EUS examination of the upper GI tract (including biliary tree) regardless of the indication.

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### GI Assistants' Evaluation of the Impact of Hands-On Practice Workshop for ERCP Training

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**Purpose:** A successful ERCP requires close coordination between endoscopist and assistant. This study evaluates GI assistants' assessment of a hands-on practice workshop with mechanical simulators for ERCP training.

**Methods:** GI assistants (nurses/techs) attended a full day training workshop with didactic talks and hands-on practice with different accessories using mechanical simulators including insertion of catheter, guide wire exchange, basket and balloon stone extraction, biliary dilation and brush cytology, placement of plastic stent and mechanical lithotripsy. An expectation questionnaire described by Borkovec et al was modified for mechanical ERCP simulator practice. Questions included: 1. How logical does this type of simulator practice seem to you? 2. How confident would you be that this simulator practice would be successful in improving your ERCP skills? 3. How confident would you be in recommending simulator practice to colleagues who are learning to perform ERCP? 4. Would you be willing to undergo proposed simulator training for improving your ERCP skills? 5. How successful do you feel this type of simulator practice would be in enhancing the skills of a different endoscopic procedure (e.g. polypectomy, esophageal stenting, etc)?

**Results:** 62 GI assistants attended 2 workshops and completed pre and post practice evaluations. There was a significant increase in mean total credibility score reported (pre  $41.0 \pm 1.3$  versus post  $46.7 \pm 0.6$ ,  $P < 0.05$ , paired t test). The assistants were confident that simulator practice would be successful in improving their skills in assisting with ERCP and that they would recommend this mode of practice to others.

**Conclusion:** Hands-on simulator practice offers GI assistants an opportunity to learn to assist with different ERCP procedures. Improvement in credibility scores validates assistants' endorsement of this mode of training.

#### Pre and Post Credibility Scores

	Q1	Q2	Q3	Q4	Q5	Total
Pre	$8.0 \pm 0.3$	$7.7 \pm 0.3$	$7.7 \pm 0.3$	$9.1 \pm 0.2$	$8.5 \pm 0.3$	$41.0 \pm 1.3$
Post	$9.3 \pm 0.1$	$9.0 \pm 0.2$	$9.4 \pm 0.1$	$9.6 \pm 0.1$	$9.4 \pm 0.2$	$46.7 \pm 0.6$
P	$< 0.05$	$< 0.05$	$< 0.05$	$< 0.05$	$< 0.05$	$< 0.05$

Data (mean  $\pm$  SEM),  $P < 0.05$  is significant

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### Longitudinal Study of Endoscopic Ultrasound-Guided Celiac Plexus Blockade (EUS-CPB) for Treatment of Painful Chronic Pancreatitis (CP)

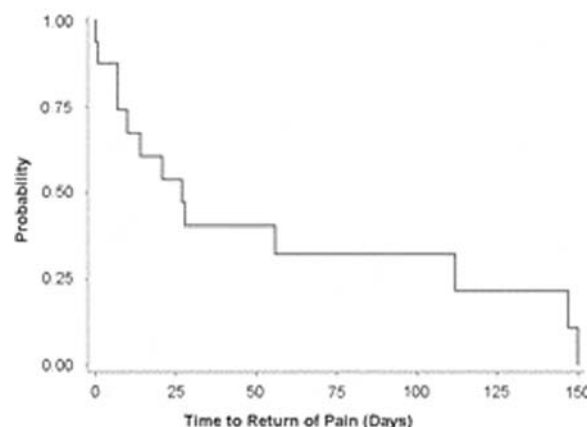
Tyler Stevens, MD\*, Gregory Zuccaro, MD, John A. Dumot, DO, John J. Vargo, MD, MPH. Gastroenterology and Hepatology, Cleveland Clinic Foundation, Cleveland, OH.

**Purpose:** To prospectively evaluate efficacy and duration of pain relief and change in opioid consumption obtained by EUS-CPB in pts with CP.

**Methods:** Consecutive pts who underwent EUS-CPB (triamcinolone/bupivacaine) for pain from suspected or established CP were enrolled into a prospective registry. Information regarding demographics,

imaging severity, opioid consumption (morphine equivalents, MEs), and EUS technique was collected at baseline. Pts were phoned 7 days post procedure to assess pain relief based on a 4-point scale (none, minimal, moderate, and complete) and post-procedure daily MEs. Duration of relief (time to return to baseline pain) was assessed through subsequent telephone contact and review of medical records.

**Results:** 26 pts underwent EUS-CPB between December 2005 and May 2007. 16 (62%) had pain relief (4 minimal, 4 moderate, 8 complete). No significant change was observed in daily MEs (mean difference 15 mg,  $P = 0.43$ ). Among the 16 responders, the median duration of pain relief was 27 days (range 1 to 150 days). [figure 1] Univariate analysis did not reveal differences in response based on age ( $P = 0.66$ ), alcohol abuse ( $P = 0.11$ ), baseline opioid consumption ( $P = 0.40$ ), imaging severity (minimal change vs. calcific,  $P = 0.89$ ), or EUS technique (unilateral vs. bilateral,  $P = 0.85$ ).



**Conclusion:** Most patients with CP have at least a partial response to EUS-CPB. However, the duration of response is short (~1 month) and opioid consumption does not change.

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### Magnetic Resonance Cholangiopancreatography Versus Endoscopic Retrograde Cholangiopancreatography in the Evaluation of Patients with Suspected Biliary Strictures and Choledocholithiasis

Emad Qayed, MD, Qiang Cai, MD, FACP\*

**Purpose:** To determine the diagnostic accuracy of magnetic resonance cholangiopancreatography (MRCP) in the detection of biliary strictures and choledocholithiasis using endoscopic retrograde cholangiopancreatography (ERCP) as the gold standard.

**Methods:** The medical records of patients who underwent both ERCP and MRCP for the evaluation of suspected biliary disease between January 2002 and January 2007 were retrospectively reviewed. Patients who had a final diagnosis of primary sclerosing cholangitis, pancreatic duct obstruction or biliary tract anomalies were excluded. Patients who underwent ERCP with stenting before the MRCP were also excluded. In all patients the presence or absence of choledocholithiasis and biliary strictures, as determined by MRCP, was correlated with the final diagnosis obtained from ERCP.

**Results:** 94 patients met the enrollment criteria of the study. The diagnoses on ERCP were choledocholithiasis in 27 patients, benign and malignant strictures in 34 patients and normal bile ducts in 33 patients. MRCP diagnosed choledocholithiasis with a sensitivity of 89%, specificity of 90% and accuracy of 89%. It resulted in seven false positive and three false negative findings when compared with ERCP. MRCP diagnosed the presence of strictures with a sensitivity of 91%, specificity of 98% and accuracy of 96%. It resulted in one false positive and three false negative findings. The overall sensitivity, specificity and accuracy of MRCP in the detection of bile duct lesions were 90%, 76% and 85%, respectively.

**Conclusion:** In this retrospective study, MRCP accurately detected the presence or absence of biliary strictures and choledocholithiasis, with a superior accuracy in detecting biliary strictures. However, the overall accuracy of MRCP (85%) in the evaluation of these biliary lesions was somewhat lower in our patient population than what is reported in other comparative studies.

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### The Severity of Pancreatic Ductal Changes on Standard MRCP According to Cambridge Classification Correlate with the Maximum Bicarbonate Level Achieved during Secretin Stimulated Exocrine Pancreatic Functional Testing (ePFT)

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**Purpose:** MRCP has shown comparable results to ERCP in detecting pancreatic ductal changes of chronic pancreatitis. ePFT is regarded as the gold standard for the detection of exocrine pancreatic insufficiency. The aim of this study is to evaluate the correlation between the severity of pancreatic ductal changes on MRCP according to Cambridge classification and the maximal bicarbonate levels achieved during secretin stimulated ePFT.

**Methods:** We retrospectively reviewed all the charts of patients who had secretin stimulated ePFT at our institution between January 2005 and March 2007. All patients who had MRCP and ePFT within four weeks time period were included in the study. All secretin stimulated ePFTs were performed in our endoscopy unite. The MRCP images were evaluated by our radiologist, who was blinded to ePFT results. Ductal changes of the pancreatic gland were assessed.

**Results:** 62 patients had ePFT at our institution between January 2005 and March 2007. 38 patients underwent MRCP and ePFT within four weeks time period. MRCP images revealed abnormal pancreatic ductal changes consistent with chronic pancreatitis (ranging from equivocal to severe according to Cambridge classification) in 16 patients. On ePFT testing 26 patients had maximum bicarbonate level above the cut off value of 80 mmol/L, and 12 patients had maximal bicarbonate level of 80 mmol/L or less. A strong correlation was found between the level of bicarbonate concentration on ePFT and MRCP scores according to Cambridge classification (Spearman 0.639,  $P$  value 0.00001), also there was a significant difference between the mean values of the maximum bicarbonate results during ePFT in patients with normal (Cambridge 0) and patients with equivocal/abnormal (Cambridge 1–4) MRCP findings (Mann-Whitney Test,  $P = 0.0001$ ).

**Conclusion:** A high degree of correlation exists between the pancreatic ductal changes as measured on MRCP according to Cambridge classification and maximum bicarbonate level achieved during ePFT testing. Further studies are needed to validate this correlation in a prospective manner.

Difference in maximum HCO<sub>3</sub> concentration according to MRCP findings

MRCP	N	Mean HCO <sub>3</sub> (SD)	$P$ value
Cambridge 0	22	106.27 (26.3)	0.0001
Cambridge 1–4	16	73.25 (19.4)	

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### Asymptomatic Common Bile Duct Dilatation in Chronic Hepatitis C Patients on Methadone

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**Purpose:** An estimated 3.9 million Americans are infected with Hepatitis C Virus (HCV) with a particularly high incidence in US veterans. The risk of Hepatitis C progression to cirrhosis is estimated to be approximately 30 percent. Chronic HCV is a known cause of hepatocellular carcinoma (HCC). Overall lifetime risk of HCC in patients with Hepatitis C cirrhosis approaches 20%. Therefore, routine screening for HCC in HCV cirrhotic patients via imaging/AFP monitoring has become standard of care with the goal of diagnosing early HCC. In the course of performing HCC screening, we have found several patients with asymptomatic common bile duct (CBD) dilatation (>6 mm) whose workups did not reveal any underlying CBD obstruction. Further evaluation showed that these patients were on methadone. It has been known for many years that narcotics, particularly, morphine can increase sphincter of Oddi pressures. A causal association between CBD dilatation and methadone use has also been previously observed in two reports in the English language with a total of 9 patients.

**Methods:** Retrospective review of veterans with HCV undergoing HCC surveillance in a major metropolitan VA medical center.

**Results:** A total of 512 patients with HCV who underwent HCC screening with abdominal sonograms were reviewed. Fifteen patients were found to have asymptomatic CBD dilatation out of which 12 (80%) were on methadone. Of the total population screened only 12.7% ( $N = 65$ ) were on methadone. The rate of asymptomatic CBD dilatation in methadone vs. non-methadone users was then analyzed. Out of 65 patients on methadone, 18.5% ( $N = 12$  patients) (mean age  $58 \pm 8.6$ ) had asymptomatic CBD dilatation (mean  $9.8 \text{ mm} \pm 2$ ), compared to only 0.67% ( $N = 3$  patients) in the 447 patients not on methadone. All patients in the methadone group with asymptomatic CBD dilatation had a normal alkaline phosphatase except for two patients, both of whom had either a normal ERCP or MRCP. The mean bilirubin was  $0.8 \pm 0.5$ , with 2 patients having total bilirubin of 2 and 1.7, both of which were due to elevated indirect bilirubin. Only 2 out of the 12 patients had cholelithiasis.

**Conclusion:** Chronic methadone use can predispose to asymptomatic common bile duct dilatation. Invasive workups may be unnecessary in methadone users with asymptomatic CBD dilatation undergoing HCC screening in the absence of clinical suspicion of bile duct pathology.

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### Hypertriglyceridemic Acute Pancreatitis Is Different

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**Purpose:** Although hypertriglyceridemia is a well known cause of acute pancreatitis, there are a limited number of studies characterizing hypertriglyceridemic acute pancreatitis (HAP). The aims of this study were to: a) compare the clinical course and severity of HAP and acute pancreatitis (AP) secondary to other causes, b) determine whether the admitting triglyceride level influences or predicts the course of HAP, c) determine how the severity of HAP in patients with diabetes mellitus (DM) compares to non-diabetics and d) evaluate serum amylase and lipase values in HAP.

**Methods:** During a 5 year period all inpatients discharged with pancreatitis and hypertriglyceridemia from two tertiary academic hospitals were identified using ICD-9 codes 577.0 and 272.1 respectively.

**Results:** 2,576 episodes of pancreatitis were identified. A cohort of 27 episodes (1.04%), comprising the fourth largest series of patients with AP attributable to HAP is characterized and described. Patients with HAP were younger ( $38.15 \pm 11.24$  years) compared to those with AP ( $45.78 \pm 13.87$  years,  $p < 0.005$ ) and had longer hospitalizations ( $10.44 \pm 8.23$  days vs.  $3.96 \pm 6.83$  days,  $p < 0.0001$ ). The mean admission triglyceride level was  $4,680 \pm 3,007 \text{ mg/dL}$  (range 728–11,554 mg/dL). There was no correlation between the admission triglyceride level and severity of pancreatitis (determined by APACHE II score, hospital LOS, and ICU LOS) in HAP patients. APACHE II scores of non-diabetics with HAP were lower compared to diabetics with HAP ( $3.11 \pm 2.85$  v.  $6.06 \pm 3.54$ ). However, non-diabetics with HAP had longer hospitalizations ( $12.67 \pm 12.70$  days) and required

more ICU care ( $5.33 \pm 7.47$  days) compared to patients with HAP and DM ( $9.33 \pm 4.87$  hospital days and  $2.56 \pm 3.92$  ICU days). The mean admission lipase value in patients presenting with HAP was  $2,507 \pm 3,689$  U/L and mean amylase value was  $266 \pm 267$  IU/L. Serum amylase values were normal in 33% of the HAP cohort, 30% of the cohort had normal lipase values, and 11% of the cohort had both normal amylase and lipase values.

**Conclusion:** Patients with HAP were significantly younger and the length of their hospitalization was significantly longer compared to patients with non-HAP. Although 66% of HAP patients had diabetes mellitus, the longer hospitalizations associated with HAP were not attributable to DM. Up to one-third of HAP patients have a normal admission amylase or lipase value and admission lipase values are generally much higher than amylase values.

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### The Effects of Alcohol and Substance Abuse on Sedation during ERCP

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**Purpose:** Unsuccessful conscious sedation is a limiting factor in endoscopic retrograde cholangiopancreatography (ERCP). Some patients become agitated and combative during the procedure. Alcohol and substance abuse may precipitate these reactions. This study was designed to investigate the effects of alcohol and substance abuse on conscious sedation for ERCP.

**Methods:** A retrospective chart review of all patients from the Veterans Administration Hospital in Memphis, Tennessee who underwent ERCP from January 2002 until December 2006 were evaluated.

**Results:** 271 ERCP procedures were done during this timeframe. The indications for the ERCP ranged from diagnostic studies to therapeutic interventions. Benzodiazepines, narcotics, and anti-emetics were used for conscious sedation. This study shows that there is a statistically significant inverse correlation between a history of alcohol and substance abuse and success with conscious sedation during ERCP. Chi-square analysis indicates a statistically significant inverse correlation between a history of alcohol use and success with conscious sedation during ERCP ( $P = 0.0131$ ). In addition, there is a statistically significant inverse correlation between a history of illicit drug use and success with conscious sedation during ERCP ( $P = 0.0021$ ). Furthermore, the lack of illicit drug use was also found to be an independent predictor of success ( $P = 0.0101$ ).

The Effects of Alcohol and Substance Abuse on Sedation During ERCP

	Unsuccessful Sedation	Successful Sedation
Current Alcohol Use	12	34
No History of Alcohol Abuse	27	198*
History of Illicit Drug Use	8	11
No History of illicit Drug Use	31	221**

\* $P = 0.0131$  \*\* $P = 0.0021$

**Conclusion:** This study found that alcohol and substance abuse correlated with unsuccessful sedation during ERCP. In this patient population, general anesthesia may be a safer and more beneficial alternative to conscious sedation.

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### Hepatic Resection Is a Safe and Effective Treatment for Bilateral Hepatolithiasis

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**Purpose:** The aim of this study was to evaluate the perioperative and long-term results of hepatectomy for bilateral hepatolithiasis comparing to that for unilateral hepatolithiasis.

**Methods:** From 1985 to 2006, 30 patients underwent hepatectomy for hepatolithiasis, and their medical records were reviewed retrospectively for immediate (operative morbidity and mortality) and long-term (stone recurrence and survival) results.

**Results:** For the patients with unilateral hepatolithiasis, left side hepatectomy was performed in 19 cases (76%) and right side hepatectomy was performed in six cases (24%). Hepatectomy to bilateral lobes was done in three of five patients with bilateral hepatolithiasis. In the other two patients, left side hepatectomy was done and the stones of the preserved liver were eliminated intraoperatively. All the stones were removed except in a patient who underwent lateral segmentectomy for bilateral hepatolithiasis. The most frequent operative complication was biliary fistula, observed in six patients. The operative morbidity was 33.3% (32% in the unilateral stone group, 40.0% in the bilateral stone group) but there was neither operative nor hospital death. History of biliary surgery was significantly correlated with the immediate operative morbidity though the other examined factors were not (e.g. location of stones, resected side of the liver, hemihepatectomy or not). With a median follow-up of 163 months (range 4 to 290), no stone recurrence or no repeated cholangitis was observed in 29 patients after complete removal of the stones. Though one episode of cholangitis, ileus, and duodenal ulcer were observed, respectively, they were treated conservatively. Two patients died of recurrence of the liver cancer coexisting at the operation, cholangiocarcinoma and hepatocellular carcinoma, respectively. One patient died of HCV liver cirrhosis. Two patients died of unrelated malignancy (gastric cancer and lung cancer).

**Conclusion:** Hepatic resection is a safe and effective treatment not only for unilateral but also for bilateral hepatolithiasis since it has high stone clearance rate and good long-term results. It might be applied carefully for patients with previous biliary surgery, the risk factor for higher incidence of immediate morbidity.

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### Two Simple Vital Sign Measurements Plus Serum Albumin Are Strong Predictors of Disease Severity in Acute Pancreatitis?

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**Purpose:** Acute Pancreatitis is one of the common causes of hospital and Intensive care unit admission. It is a potentially serious disease and with Intensive Care Management lead to decrease in mortality. The aim of this study was to determine if simple vital sign measurements combined with routine lab results can identify acute pancreatitis patients who will be transfers to the ICU.

**Methods:** All patients admitted and diagnosed with acute pancreatitis (2005-2006) were included (N = 101). Data collected were CBCs, SMA7s, LFTs, serum albumin and vital signs [blood pressure, respiratory rate (RR), pulse rate (PR) and temperature (T)] on admission, after 24 and 48 hrs. Severity of disease was classified based on outcome [hospital discharge vs. transfer to intensive care (ICU)].

**Results:** Patient mean age was  $57 \pm 17$  (sd) years (range = 28-97 yrs), 45% were females and 24% of the sample were transferred to the ICU. Preliminary statistics (student t-tests & chi-square analysis) identified a number of variables to be associated with ICU transfer (low and/or worsening albumin, elevated Temperature, PR > 89, elevated amylase and/or lipase) and others that were not (remaining CBCs, SMA7s and vital signs). A logistic regression model to predict ICU transfer was then developed including age, sex and either absolute or trend variables (increasing or decreasing values during 48 hrs) for labs and vital signs (step-wise addition). This approach

identified three strong predictors of ICU transfer; a 92% decreased risk of ICU transfer for every 1.0 g/dL ( $>1.6$ ) increase in albumin by 48 hrs ( $P = .014$ ), a 9-fold increased risk of ICU transfer with a  $PR > 89$  at 48 hrs ( $P = .027$ ) and a  $T > 98.6^\circ F$  at 48 hrs ( $P = .017$ ). With the inclusion of these three predictors to the model no other lab or vital sign measurement were found to predict ICU transfer. Early ICU management lead to decrease mortality from 25% to less than 10%. This model had an overall specificity of 93% with positive and negative predictive values of 75% and 85%, respectively. Patients which were transferred to ICU also meet other Prognostic criteria such as (Ranson's and APACHE-II).

**Conclusion:** These findings suggest that careful monitoring the changes in body temperature, pulse rate and albumin status during the initial 48 hours following admission can accurately predict patients at risk for ICU transfer. Monitoring these markers shown decrease mortality from 25% to less than 10%.

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### Comparison of Abdominal Ultrasound and ERCP in Determining the Etiology of Obstructive Jaundice

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**Purpose:** ERCP remains the gold standard for diagnosis and initial treatment of patients with obstructive jaundice. Accuracy of ultrasound in such patients and its concordance with ERCP has not been studied in our part of the world. Objective: To compare the efficacy of abdominal ultrasound and ERCP in determining the etiology of obstructive jaundice

**Methods:** Study was carried out at a tertiary care referral center in Lahore, Pakistan from August 2006 to May 2007. Patients undergoing ERCP for provisional diagnosis of obstructive jaundice were included. Abdominal ultrasonographic examination was conducted before ERCP and all patients underwent ERCP under conscious sedation. Diagnosis on ultrasound and ERCP was compared using cross tabulation.

**Results:** A total of 54 patients (male: female ratio of 0.6 (22/32)) with a mean age of 47.22 ( $\pm 14.94$ ) were included in the study. Jaundice and Abdominal pain were the predominant presenting symptoms in 48 (88.9%) and 42 (77.8%) patients respectively whereas pruritis and fever were present in 27 (50%) and 11 (20.4%) patients respectively. Choledocholithiasis/sludge was accurately diagnosed in 8 out of nine patients. Ultrasound only diagnosed 50% of the patients with Peri-ampullary tumors and pancreatic carcinoma accurately; sonographic finding of a distal CBD stricture without any definitive diagnoses were noted in the rest of the patients. Ultrasound was very accurate in determining the etiology of various proximal CBD lesions. In the 4 patients with mid-CBD strictures on ultrasound, 2 were found to have gall bladder carcinoma, 1 common hepatic duct stricture and 1 acute pancreatitis- diagnoses which are not usually possible on ERCP. Of the 3 patients with Cholangiocarcinoma, 2 cases had been suspected to have this diagnosis on ERCP and ultrasound alike while the third one had a mid-CBD stricture on ultrasound. Ultrasound findings had complete concordance with the ERCP diagnoses in cases of post-cholecystectomy strictures, fistulas and CBD ligation.

**Conclusion:** Ultrasound was very accurate in determining the etiology of various proximal CBD lesions.

The accuracy of Ultrasound in determining the etiology of distal biliary obstructive processes is significantly lower but is useful as initial investigation. Abdominal ultrasound and ERCP are complementary investigations in patients with obstructive jaundice.

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### Prevalence of Fungal Infection in Patients with Severe Acute Pancreatitis and Its Outcome

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**Purpose:** The present prospective study was aimed at exploring prevalence of fungal infections in patients with SAP, to detect predisposing factors for the same and to study the outcome of these patients.

**Methods:** Fifty consecutive patients with SAP were investigated for evidence of fungal infection (F I) by culture of blood, urine, drain fluid (if instituted) on day 0, 7, 14 and 21 days and thereafter if indicated and culture of fine needle aspirate (FNA) from pancreatic / peripancreatic tissue and samples collected at necrosectomy. All patients were managed with broad spectrum antibiotics, parenteral or naso-jejunal feeding and supportive care. Patients with fungal infection were treated with amphotericin or fluconazole.

**Results:** The etiology of SAP in 50 patients (mean age 39.66 yr; 37 males) was alcohol 29 (58%), gallstones 11 (22%) and others in 10 (20%). Fungal infection was documented in 18 (36%) patients, in 9 patients in the operative specimen, in 3 patients from the FNA sample and in 9 in the blood culture (4 patients had specimens from two sites positive). In contrast to patients without F I those with F I more often had evidence of respiratory failure ( $P = 0.031$ ) or hypotension ( $P = 0.031$ ) at admission, had prolonged hospital stay ( $P = 0.01$ ), longer duration of antibiotics ( $P = 0.003$ ), antibiotic treatment for  $> 4$  weeks ( $P = 0.042$ ), TPN ( $P = 0.005$ ), invasive interventions ( $P = 0.022$ ) and required mechanical ventilation ( $P = 0.001$ ). On logistic regression analysis the independent risk factors for fungal infection were antibiotics therapy for  $> 4$  weeks and hypotension at hospitalization. Of the 18 patients with FI, 13 received intravenous amphotericin ( $N = 7$ ) or fluconazole ( $N = 6$ ) and 8 of them survived while all 5 did not receive antifungals died; while in the non-fungal group, 21 of the 32 survived. Patients who died more often had  $> 50\%$  necrosis of the pancreas ( $P = 0.045$ ) had a higher mean APACHE II score ( $P = 0.001$ ) and respiratory failure at admission ( $P = 0.07$ ) and more often required mechanical ventilation ( $P = 0.58$ ).

**Conclusion:** 36% of patients with SAP developed fungal infection. Prophylactic antibiotic therapy emerged as a strong risk factor. Prompt institution of anti-fungal therapy improved survival in these patients.

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### Disconnected Pancreatic Duct Syndrome (DPDS) Requiring Distal Pancreatectomy Is a New Indication for Pancreatic Islet Autotransplantation (PIA): Initial Experience in 7 Patients

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**Purpose:** DPDS after severe acute pancreatitis requires distal pancreatectomy, resulting in diabetes in a third to half of patients. PIA has been reported after total pancreatectomy but not after distal pancreatectomy for DPDS. We report our initial experience with 7 (3 successful) patients.

**Methods:** Clinical, radiologic, endoscopic, and surgical details of 7 patients are shown in table.

Three of 7 patients had successful PIA (one with intrahepatic hematoma requiring transfusion and embolization). Only factor which predicted low yield was firm pancreas at surgery in 3 of the remaining 4 patients. Two of these 4 pts developed postoperative diabetes.

**Results:** See Table 1.

**Conclusion:** PIA is feasible for patients with DPDS undergoing distal pancreatectomy but low islet yield is a problem. PIA needs evaluation in larger number of patients with longer follow-up.

**Table 1.** Clinical, Endoscopic and Surgical Characteristics and Outcomes of 7 Patients Undergoing PIA

	#1	#2	#3	#4	#5	#6	#7
Age and Sex	39 M	60 F	36 F	42 M	42 M	28 F	53 F
Etiology	Biliary	Post-ERCP	Biliary	Idiopathic	Idiopathic	Idiopathic	Biliary
Interval between onset and diagnosis of DPDS (months)	12	11	15	27	13	1.25	1
Interval between diagnosis and surgery (months)	12	1	0	4	11	5	4
Preop diabetes	+	+	—	—	—	—	—
Preop narcotics	+	+	—	+	Only for attack	+	+
Endoscopic, Surgical, and Pathologic Characteristics of Patients							
Pre-endoscopic fluid collection	+	+	+	+	+	+	+
# Endoscopic interventions	7	2	5	12 (1 after surgery)	4	6	2
% resection	50	70	80	60	50	50	70
Pathology	CP	CP	CP	Negative for tumor	CP	CP	CP
Clinical, Radiologic, and Endocrine Outcomes							
Total Ischemic time (hours)	0.75	1.75	1.8	0.75	2.0	1.5	2.0
Islet Equivalents	62,837	183,833	135,043	420	No islets	3563	3643
Pain Relief	No narcotic	No narcotic	No narcotic	No narcotic after few weeks	Acetaminophen	On narcotic	No narcotic
Post-surgery fluid collections	No	Yes, small	Yes	+ Yes, ERCP for leak	?	No	No
Postop diabetes	+ (insulin)	—	—	+	—	—	+

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**Bouveret's Syndrome**

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**Purpose:** 81 y/o Caucasian male with past medical history significant for Cholecystitis (25 yrs ago), Diabetes, HTN and hypothyroidism (on replacement) presented to the ER with sudden onset of severe nausea and vomiting (15 episodes) of 1 day duration. Vomited brownish liquid. Denied any frank blood. Denied any abdominal pain, bloating, diarrhea, constipation, weight or appetite changes. Patient does describe of an episode of right upper quadrant pain 25 yrs ago when he was diagnosed with with cholecystitis which was treated with antibiotics, but did not undergo any cholecystectomy at that time. Did not have any similar episodes since then. Denied alcohol use. Quit smoking 35 yrs ago. Allergic to sulfa. On examination, vitals were stable. Age appropriate male with truncal obesity in no acute distress. Abdomen was soft, non tender and non distended. No scars. Small umbilical hernia noted. No Murphy's sign. Bowel sounds were normal. No hepatosplenomegaly. No shifting dullness. Labs showed a WBC count of 20.4. Rest of CBC was normal. BMP was normal except bicarb of 35, BUN of 4 and serum creatinine of 1.8. LFTs, bilirubin and protein were within normal limits. Abdominal X ray showed a large gall stone and pneumobilia. CT abdomen with oral contrast and IV contrast showed a big gall stone of 4–5 cm in duodenum, pneumobilia, pyloric obstruction suggesting Bouveret syndrome. Treatment was started with symptomatic control with Zofran. Kept on NG suction and IV fluids. Gastroenterology and Surgery teams were consulted. Started on Zosyn empirically. It was decided to remove the stone by endoscopy and

if unsuccessful, plan was to take the patient to surgery. But subsequently GI service was able to remove the stone by endoscopic lithotripsy. Patient improved after stone removal and denied any nausea, vomiting or abdominal pain. Subsequently, patient underwent elective laproscopic cholecystectomy within 6 weeks after discharge.

**Conclusion:** 1. A timely cholecystectomy would have prevented this complication called Bouveret syndrome. We reinforce the importance of interval cholecystectomy in patients presenting with symptomatic gall stones to prevent future complications. 2. Endoscopic lithotripsy can be tried before surgical approach.

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**Prophylactic Pancreatic Stents: Benefit and Frequency of Downstream Spontaneous Migration**

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**Purpose:** The first objective was to assess the benefit of Prophylactic Pancreatic Stent (PPS) in our high risk population and the frequency of spontaneous migration of PPS. Second objective was to identify any clinical or technical factors associated with spontaneous migration.

**Methods:** We reviewed the charts and endoscopic records of all patients who received a PPS from 2002 to 2006. Data collected included gender, age, ERCP indication, procedure performed during ERCP, type of PPS, symptoms after the initial ERCP, spontaneous stent migration and the need for

endoscopic removal. Patients were classified in 2 groups according to stent outcome; spontaneous migration or endoscopic removal, with a comparison for clinical and technical characteristics. Frequency and interval to demonstrate spontaneous dislodgment or to perform endoscopic removal were recorded.

**Results:** From June 2002 to November 2006, we identified 152 PPS that were placed in 141 patients (99 women and 42 men). The average age was 48.7 years (range 19–87). Pancreatic sphincterotomy was the most common procedure performed with 71 cases. Stent average length was 3 cm. Seventeen patients (11.1%) had post-ERCP pancreatitis, with 3 severe episodes. Factors associated with higher rates of post-ERCP pancreatitis were younger age ( $P = 0.03$ ) and pancreatic sphincterotomy of the major papilla ( $P = 0.06$ ). Complete follow up data was not available in 6% of the patients. Spontaneous migration was demonstrated in 88 stents (63.3%). The remaining 51 stents (36.7%) were removed by endoscopy. No significant difference was observed between these 2 groups of patient. A trend for higher rates of spontaneous migration was noted in females ( $P = 0.06$ ). The mean delay to demonstrate PS migration was 35 days (range 2–372). Endoscopic removal was performed after a mean of 55 days (range 6–1119).

**Conclusion:** PPS placement in high risk patients reduces post-ERCP pancreatitis rate, however severe pancreatitis may still rarely occur. Spontaneous migration of PPS was observed in 63% of cases. This rate may be increased by the use of stents with smaller caliber. No clinical or technical factors were identified to help to predict in which situation spontaneous stent migration will occur, except a tendency for more spontaneous migration in women. Because of poor patient compliance, long delays for the stent assessment and removal were observed.

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### Biliary Tract Complications in Orthotopic Liver Transplant Patients: A Single Center Retrospective Observational Study

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**Purpose:** Biliary tract complications (BTC) have been a significant source of morbidity after orthotopic liver transplantation (OLT). The aim of the study is to review the incidence and timing of biliary complications in patients who underwent OLT at The University of Texas Health Science Center at San Antonio (UTHSCSA).

**Methods:** 996 patients underwent OLT at our institution between November 1992 to October 2006. Those who had a T-tube placed at the donor-recipient common bile duct (CBD) anastomosis or had choledochojunostomy were excluded from our study. BTC were categorized as: i) stone/sludge; ii) sphincter of Oddi dysfunction (SOD); iii) leaks; and iv) strictures based on cholangiographic findings at ERCP. Leaks and strictures were further classified as anastomotic (A) or non-anastomotic (NA) and as early ( $\leq 90$  days post OLT) or late ( $> 90$  days post OLT).

**Results:** A total of 899 patients were included in the study, of which 223 patients (24%) underwent ERCP for suspected BTC. 190 patients (21.1%, PPV 85.2%) were found to have a BTC at ERCP. The incidence of stones/sludge, SOD, leaks and strictures were 5.3%, 3.2%, 18.9% and 72.6% respectively. Of the 36 patients with leaks; 23 were (A); 12 (NA) and 1 both. 32 presented early and 4 presented late. Of the 138 patients found to have strictures, 119 were (A); 5 (NA) and 14 both. 109 presented early and 29 late.

**Conclusion:** ERCP is an effective and accurate approach for the diagnosis of biliary tract complications after OLT. The overall BTC rate in our large series was 21%. Early anastomosis strictures were the most common BTC observed. Biliary leaks generally occurred early and at the anastomosis. Despite advances in OLT surgical techniques, BTC remains a significant source of morbidity in our post-OLT patients.

**Table 1.** Incidence of biliary tract complication in orthotopic liver transplant patients.

Total OLT	899
Total BTC	190 (21.1%)
Stones/sludge	10 (5.3%)
SOD	6 (3.2%)
Leaks	36 (18.9%)
anastomotic	23
non-anastomotic	12
both	1
Strictures	138 (72.6%)
anastomotic	119
non-anastomotic	5
both	14

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### Pancreatic Cholera

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**Purpose:** VIPoma is a rare gastrointestinal endocrine tumor seen in 1 in 10 million per year.

**Case Report:** A 37 year old African American male was initially admitted to a community hospital with diarrhea and acute renal failure (acute tubular necrosis) that required hemodialysis. At that time, he was diagnosed with inflammatory bowel disease based on nonspecific erythema on colonoscopy. He was started on mesalamine and the diarrhea improved, with recovery of kidney function. He was discharged to a rehabilitation facility. Two weeks later, he was readmitted to our hospital with large volume diarrhea. On examination he was found to be disoriented, hypotensive, tachycardic and tachypneic. Labs showed a leucocytosis  $18.4 \times 10^3/\text{mm}$ , potassium 2.7 mmol/L, BUN 83 mg/L and creatinine 17.05 mg/dl and lipase 779 U/L. ABG revealed a pH 7.1,  $\text{PaCO}_2$  7 MM/Hg,  $\text{PaO}_2$  118 MM/Hg and  $\text{HCO}_3^-$  was 2 MEQ/L. Urine sediment showed muddy brown casts. Stool cultures were negative. Stool anion gap was 17. He responded well to hemodialysis and recovered his renal function. Because of the classic presentation, large volume secretory diarrhea (normal stool anion gap), we pursued investigation for possible VIPOMA.

**Workup:** CT scan of the abdomen showed 5.7 cm mass in pancreatic tail and the octreotide scan was positive in the same area. Serum VIP level was 1474 pg/ml, thus confirming the diagnosis of VIPoma.

**Management:** Octreotide 50  $\mu\text{C}$  SC every 8 hours resulted in control of his diarrhea. He underwent surgical resection of the tumor. The pathologic specimen was a neuroendocrine tumor. After surgery diarrhea ceased.[figure1]



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**Blunt Trauma to the Main Pancreatic Duct: Cut or Stent?**

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**Purpose:** Blunt injury to the main pancreatic duct is commonly a result of motor vehicular accident, trauma, or assault involving the upper abdomen. With better imaging modalities now available, exploratory laparotomy is not always necessary to make this diagnosis. However, there is little published data to help decide the best course of action in the pancreatic duct when surgical therapy is not needed for other concomitant injuries. We wanted to determine which approach has led to the best outcome at our institution in treating cases of blunt injury to the pancreatic duct.

**Methods:** We reviewed the charts of patients admitted to our institution between 2001 and 2006 who experienced blunt trauma to the pancreatic duct.

**Results:** A total of eight cases were studied. One was lost to follow up after transfer to another facility. Of the remaining seven patients, only one had a pancreatic stent placed within 72 hours of the injury. This patient was able to tolerate oral intake within 48 hours of the stent placement and was discharged from the hospital five days after the injury. He has been doing well for over six months and the stent has been removed. The remaining six patients underwent distal pancreatectomy and had a median hospital stay of 45 days for the original injury and its complications. Complications occurred in five of these six patients (83%) in this group and included pancreatic abscess, pseudocyst, and fistula. One patient continued to show copious leakage of pancreatic juice into the abdominal cavity during the observation period. Stent placement was attempted two weeks after the initial injury, but it was not successful because the proximal part of the main duct was closed off by then. Pancreatic juice leakage and saponification made the surgical therapy technically difficult. Distal pancreatectomy was associated with significant morbidity on a long-term basis. Pancreatic stent placement within 72 hours of the injury to the main pancreatic duct produced the best outcome, avoiding distal pancreatectomy and such consequences as diabetes.

**Conclusion:** At our facility, the best course of action in cases of blunt trauma resulting in injury to the main pancreatic duct is placement of a pancreatic stent to seal the leak within 72 hours of the injury. This early endoscopic intervention was associated at our institution with a shorter hospital stay and much less short-term and long-term morbidity compared to distal pancreatectomy. This is our institutional experience and larger prospective studies are needed to confirm our findings.

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**Prevalence of Gall Bladder Dyskinesia in Gastroparesis**

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**Purpose:** The aim of this study is to assess the gall bladder ejection fraction (GBEF) by cholescintigraphy in a cohort of gastroparetic patients with prominent postprandial abdominal pain.

**Methods:** 17 patients with gastroparesis (14 females) underwent the hydroxyl iminodiacetic acid (HIDA) scan to measure their GBEF over the last 2 years. A GBEF between 35%–50% on the HIDA scan was considered as a borderline positive test for gall bladder dysmotility and a GBEF <35% was considered as definite evidence of gall bladder dyskinesia. Gastroparesis for this study was defined as retention of >10% of a standardized low fat isotope labeled egg beater meal at the end of 4 hours by scintigraphy. Demographic data, the etiology of gastroparesis, duration of gastroparetic symptoms, and bowel movement pattern were also recorded.

**Results:** 11/17 (65%) of patients had a GBEF of <50%, 8 of these patients had definite evidence of gall bladder dyskinesia, while the other 3 had a borderline positive test. 7/8 patients with a definitely positive test underwent cholecystectomy, of which 5 had chronic cholecystitis on pathology. 6/7 patients reported improvement in pain after the cholecystectomy. None

of the patients with borderline evidence of gall bladder dysmotility underwent cholecystectomy. Clinical characteristics of patients are summarized in table. There was no significant difference ( $p > 0.05$ ) in age, or duration of gastroparetic symptoms in patients with normal and abnormal gall bladder ejection fraction. Gall bladder dysmotility was numerically more likely in females (OR 5; 95% CI: 0.35–72%), idiopathic gastroparesis (OR 5; 95% CI: 0.6–46), and in patients with constipation (OR 2; 95% CI: 0.2–13).

**Conclusion:** 1) This pilot study shows that gall bladder dysmotility is present in a majority of patients with gastroparesis; particularly of idiopathic etiology. 2) Underlying neuromuscular dysfunction in gastroparesis may also extend to the gall bladder, consistent with a neuropathic etiology to explain the gall bladder dyskinesia. 3) Appreciating the need to diagnose and treat biliary dyskinesia in gastroparesis could be an important strategy to address the pain component in this challenging clinical setting.

Clinical Characteristics of gastroparetic patients who underwent HIDA scan

Characteristic	Gastroparesis with gall bladder dysmotility n (%)	Gastroparesis without gall bladder dysmotility n (%)
Etiology:		
Diabetes Mellitus	2 (18%)	3 (50%)
Idiopathic	8 (72%)	2 (33%)
Age (years)	40 (33–47)	38 (28–48)
Duration of gastroparetic symptoms (years)	4 (2–6)	7 (3–11)

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**Long-Term Follow up of Endoscopic Sphincterotomy for Bile Duct Stone Removal: A North American Perspective**

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**Purpose:** Endoscopic sphincterotomy for stone removal is commonly performed for bile duct stones with early morbidity in about 10% of patients. Late-occurring complications occur in 3% to 24% of patients in Asian and European studies. There are no published data on long-term outcomes from North America. The aim of this study is to determine the long term outcomes of endoscopic sphincterotomy for bile duct stones in a North American population.

**Methods:** Patients who had endoscopic sphincterotomy for stones between 1991 and 2000 were identified from billing records at the University of Utah Health Sciences Center and those with 5 or more years follow up were included. Patients with sphincterotomy for other indications were not included. Living participants were contacted by phone to complete a questionnaire regarding their biliary and pancreatic health, and the next of kin responded for the deceased. Chart review was also performed. Any complications that developed more than 30 days post-procedure were considered late-occurring.

**Results:** 193 individuals were identified who met inclusion criteria, including 43 individuals who were deceased. Follow up was possible on 80 (41.5%) individuals including from the relatives of 26 who were deceased. The mean duration of follow up was 7.75 (range, 5 to 14) years. There were 43 females and 37 males with a mean age of 62 (range, 23–94) years. Cholecystectomy was performed in 22 (27.5%) individuals prior to ERCP and 30 (37.5%) afterwards. Eight (10%) persons had late-occurring complications (Table 1). There were no cases of cholangiocarcinoma. All complications occurred in those who had undergone cholecystectomy before, or within 14 days after sphincterotomy, and no one had multiple complications. None of the deceased patients had known pancreatobiliary complications and all died of unrelated causes. No patient required surgery, radiographic therapy, prolonged hospitalization or ICU care, and there were no sphincterotomy-related deaths.



**Conclusion:** In a North American population, endoscopic sphincterotomy for bile duct stones is associated with complications in 10% of patients over the long-term, which is comparable to reports from Europe and Asia. These complications are usually mild and treatable with ERCP.

Late-occurring Complications of ERCP with Sphincterotomy for Bile Duct Stones

	Number	ERCP #
Pain	3	1/0/0
Stones	2**	1/1
Orifice Stenosis	2	1/4
Pancreatitis	1***	0

\*\*Occurred 2 and 7 years post-ERCP

\*\*\*Required 1 day hospitalization

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### Perceived Cancer Risk among Patients with Pancreatic Cysts

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**Purpose:** The natural history of pancreatic cystic neoplasms has not been clearly defined and currently available techniques are at times inadequate for differentiating premalignant cysts from benign cysts. Therefore, surveillance of these patients is of paramount importance. We conducted a questionnaire study to evaluate patients' knowledge of pancreatic cysts and their perceived risk of developing pancreatic cancer.

**Methods:** Sixty-eight consecutive patients evaluated by EUS for a pancreatic cyst from 2005 to 2006 were contacted by telephone to administer the questionnaire. Their knowledge of the pancreas and pancreatic cysts was evaluated. Patients were asked to estimate their risk of developing cancer from the cyst over 5 years and if they believed surveillance was necessary. Based upon clinical and endoscopic parameters, each patient's risk of cancer was also estimated by three experienced gastroenterologists who were blinded to each other and patient responses. Following arrival at a consensus opinion regarding each individual's risk for cancer development the agreement in risk perception between patients and the expert panel was assessed by the weighted kappa statistic.

**Results:** A total of 48 (71%) patients with pancreatic cysts were successfully contacted. Only 14 (29%) knew what the function of the pancreas was and 10 (21%) were able to identify the type of cyst they were diagnosed with. The three gastroenterologists completely agreed or had minor disagreement in 87% of cases and the kappa value between each pair of gastroenterologists ranged from 0.69 to 0.77 (good). Agreement between each patient and the expert panel's consensus cancer risk was mediocre (kappa of 0.30). Of 16 patients who believed their cancer risk was "zero", the expert panel agreed in only 4 cases. Among 32 patients who had at least a "very small" risk of cancer and would be recommended to undergo surveillance, only 60% believed surveillance was necessary.

**Conclusion:** The definitive diagnosis and subsequent treatment of pancreatic cystic neoplasms is still poorly defined. If resection is not performed, surveillance may be essential to protect from later cancer development. Most patients with these lesions do not have an adequate understanding of the pancreas or pancreatic cystic neoplasms. Furthermore, there is mediocre agreement between gastroenterologists and patients regarding their cancer risk. Patients' low perceived risk of cancer may have a negative impact on subsequent adherence to surveillance recommendations.

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### Trends and Experiences with ERCP and MRCP in Maryland

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**Purpose:** To define practice patterns and perceptions regarding ERCP and MRCP among community based gastroenterologists in the state of Maryland.

**Methods:** A survey consisting of 31 multiple-choice and free text entry questions was developed using a commercial survey website. Questions about training and utilization of ERCP, perception and utilization of MRCP, and practice setting were included. The survey was sent by email to Maryland members of the ACG, AGA, and ASGE. Physicians with email addresses from academic institutions were excluded.

**Results:** Forty-nine gastroenterologists completed the survey. Twenty-eight (57%) currently perform ERCP. During fellowship, 5 (18%) performed >200 cases and 18 (64%) performed <100 cases. Six (21%) completed an additional year of advanced endoscopic training. Thirteen (46%) reported an annual volume of <50 cases and 11 (39%) reported an annual volume of 50 to 100 cases. One reported an annual volume of >200 cases. All perform ERCP for treatment of obstructive jaundice, choledocholithiasis, and cholangitis. Nineteen (67.9%) perform ERCP for diagnosis of suspected pancreatic or biliary tract disease and 22 (78.6%) perform ERCP to establish the diagnosis of choledocholithiasis. ERCP volume decreased since entering practice for 16 (57%). Fourteen (87.5%) attributed the decrease to the introduction and expanding role of MRCP and most (89.3%) believe the technology has altered their practice. Respondents feel ERCP findings correlate with MRCP findings always, most of the time, or sometimes in 4%, 68%, and 28% of cases. Of the 21 not currently performing ERCP, 10 (48%) performed ERCP previously, half within the last 5 years. Common reasons for abandoning the practice of ERCP were decreasing comfort level (60%), time constraints (50%), fear of procedural complications (40%), unfamiliarity with new technology (20%) and fear of litigation (20%).

**Conclusion:** In the state of Maryland, most surveyed gastroenterologists performed less than the currently recommended 180–200 ERCP's during fellowship and nearly all perform < 100 ERCP's annually. MRCP has decreased ERCP volume for most. Despite the belief that MRCP has altered practice and the feeling that MRCP findings correlate with ERCP findings most of the time, many still perform ERCP for diagnostic purposes. Those who abandoned the practice of ERCP did so mostly due to time constraints, decreasing comfort with the procedure, and fear of complications. A nationwide survey is planned.

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### Acute Experimental Pancreatitis in Rats Is Ameliorated by Treatment with Pramlintide, a Synthetic Analogue of the $\beta$ -Cell Hormone Amylin

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**Purpose:** Acute pancreatitis is a common and major complication of endoscopic retrograde cholangiopancreatography (ERCP) and limits the use of this otherwise safe procedure. Antisecretory drugs such as somatostatin (SST) and its long-acting analogue octreotide, or protease inhibitors such as gabexate mesilate, have been tested as therapies for pharmacological prevention of post-ERCP pancreatitis, but uncertainty still exists over their clinical benefit. At physiologically relevant doses in animal models, the  $\beta$ -cell hormone amylin slows gastric emptying, inhibits gastric acid secretion and exocrine pancreatic secretion, and protects the gastric mucosa. The present study examined the effect of pramlintide (pram), a synthetic human amylin analogue, on prevention of caerulein-induced acute pancreatitis in anesthetized Sprague Dawley<sup>®</sup> (SD) rats.

**Methods:** Saline, pram (300  $\mu$ g/kg/h), SST (10  $\mu$ g/kg bolus) or pram+SST in combination (N = 16, 5, 5, 6, respectively) was infused intravenously from 30 min before until 240 min after caerulein IP injection (10  $\mu$ g/kg) into fasted, male, anesthetized SD rats (320–360 g). As an index of acute pancreatitis, plasma lipase and amylase were measured for up to 240 minutes after caerulein injection.

**Results:** Following caerulein injection, plasma amylase increased 2.23-fold at 240 min in saline-treated controls compared to 1.40-, 1.61- and 1.51-fold in rats receiving pram, SST or the combination ( $P < 0.01$ ,  $P < 0.04$  and

$P < 0.01$ , respectively). Plasma lipase increased by 20.3-fold in the control saline group compared to 8.1-, 6.1- and 5.0-fold in pram, SST or combination groups ( $P < 0.02$ ,  $P < 0.01$  and  $P < 0.01$ , respectively). Although each was different from controls, there were no significant differences between SST, pram or pram+SST treatments in attenuating caerulein-induced increases in plasma amylase and lipase in this animal model of pancreatitis.

**Conclusion:** Pramlintide ameliorated increases in pancreatic enzyme activity in this rat model of acute pancreatitis. Future studies are warranted to explore the potential use of pramlintide in the prevention of pancreatitis, which may occur during ERCP procedures. This research was funded in part by Amylin Pharmaceuticals, Inc., San Diego, CA.

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### Trainers' Assessment of Mechanical Simulator Practice in ERCP Training

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**Purpose:** There is a paucity of simulator models for ERCP training. We explored trainers' evaluation of potential application of a mechanical simulator for ERCP practice to supplement trainees' clinical experience.

**Methods:** At 2007 DDW, ERCP trainers were introduced to new ERCP accessories by a U.S. manufacturer. Participants tested the accessories using a mechanical simulator (GIE 2007;65:1056-1062) and completed a modified expectation questionnaire (Borkovec, J Behav Ther Exp Psych 1972;3:257-260) before and afterwards. Questions were: (1) How logical does this simulator practice training seem to you? (2) How confident are you that this simulator practice would be successful in improving trainees' ERCP skills? (3) How confident would you be in recommending simulator practice to trainees who are learning to perform ERCP? (4) Would your trainees be willing to undergo simulator training? (5) How successful do you feel this simulator practice would be in enhancing skills of a different endoscopic procedure, e.g. esophageal stenting?

**Results:** Data of 12 completed sets of pre and post evaluations were analyzed using the paired t test. There was a significant increase in the mean total credibility score (Table 1) reported by the trainers (pre  $41.3 \pm 1.3$  vs post  $44.5 \pm 1.8$ ,  $P < 0.05$ ). In particular, the trainers were significantly more confident after the use of the simulator that this simulator practice would be successful in improving the trainees' ERCP skills and that they would recommend simulator practice to trainees.

**Conclusion:** Exposure to simulator practice provided trainers the opportunity to evaluate the use of mechanical simulator for ERCP training. Improvement in credibility scores validates trainers' endorsement of this mode of practice to complement clinical training. These endorsements indicate that impact of mechanical simulator practice on trainees' clinical performance deserves randomized controlled assessment.

**Table 1.** Pre and Post responses to Expectation Questionnaire and Credibility Scores

	Q1	Q2	Q3	Q4	Q5	Total scores
Pre	$8.3 \pm 0.5$	$7.2 \pm 0.4$	$8.3 \pm 0.4$	$9.7 \pm 0.2$	$7.8 \pm 0.5$	$41.3 \pm 1.3$
Post	$8.8 \pm 0.4$	$8.6 \pm 0.3$	$9.2 \pm 0.4$	$9.8 \pm 0.3$	$8.3 \pm 0.5$	$44.5 \pm 1.8$
P value	n.s.	< 0.05	< 0.05	n.s.	n.s.	< 0.05

Data expressed as mean  $\pm$  SEM,  $P < 0.05$  is significant, n.s. = not significant

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### Wire Controlled Cannulation Reduces the Risk of Post-ERCP Pancreatitis in Children by Initially Accessing the Bile Duct with a Soft-Tipped Guidewire, without Contrast Injection

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**Purpose:** Pancreatitis is the most common and serious complication of diagnostic and therapeutic ERCP, occurring in 3–30% of cases overall. However, limited data on children have been published to date. Patient factors such as age, prior history of post-ERCP pancreatitis, and technical factors (experience of the endoscopist and the number of PD injections) are high-risk predictors for post-ERCP pancreatitis. Traditional training recommendations for cannulation of the common bile with initial contrast injection are outdated and should be revised. This study asked the question: can the incidence of post ERCP pancreatitis in children be reduced by initially accessing the bile duct with a soft-tipped guidewire prior to contrast injection?

**Methods:** Retrospective assessment of all children who underwent ERCP for selective CBD cannulation by a single endoscopist from July 2002 to June 2006 was performed. All patients included had initial, selective CBD cannulation using a soft-tipped guidewire and a sphincterotome. The CBD was freely cannulated with the wire, after which time the cannulotome was advanced into the mid CBD, prior to injecting any contrast. Cases requiring minor ampullary cannulation were excluded.

**Results:** ERCP was successful in cannulation of the CBD in 99.4% of patients. A total of 162 ERCPs were performed for selective CBD cannulation over a 48 month period by single endoscopist. All procedures utilized initial wire-guided cannulation with a 0.025 soft-tipped guidewire. Two patients (1.5%) developed clinically identifiable mild post-ERCP pancreatitis; one (0.7%) developed post-sphincterotomy bleeding which did not require therapy. None had developed pseudocysts or sequelae of chronic pancreatitis up to 6 months after evaluation. There were NO cases of severe pancreatitis (0%) or ICU admissions as a result of Post-ERCP pancreatitis.

**Conclusion:** Accessing the bile duct with a soft-tipped guidewire likely significantly reduces the risk of developing post-ERCP pancreatitis in children. Further study is needed.

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### Pancreatic Cyst Size and Malignancy: An Endoscopic Ultrasound Perspective

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**Purpose:** Cysts of the pancreas are often found incidentally on many conventional radiographic imaging tests. Often, these rely on size to suggest significance.

**Methods:** A retrospective analysis of all pancreatic cysts presenting for endoscopic ultrasound examination was made. 41 consecutive patients over a period of 18 months were analyzed. Fine-needle aspiration was performed of cysts. Cyst fluid was analyzed for CEA level, amylase, and cytology along with correlation to clinical and endosonographic appearance.

**Results:** The patient group included 22 men (53.6%) and 19 (46%) women. Average age was 63 years. Of all cysts, 6 were found by histology and CEA levels to be malignant. The average size of these cysts were  $9.29 \text{ cm}^2$ . Benign cysts included 35 total with an average size of  $12.10 \text{ cm}^2$ . Of the benign cysts, 12 were found to be pseudocysts based on the above tests. The average size of pseudocysts was  $16.02 \text{ cm}^2$ . In comparison of the benign cyst size to malignant cyst size, no statistical significance was found ( $P = 0.53$ ). In comparison of all benign cysts to pseudocysts, no significant difference was identified ( $P = 0.31$ ). Additionally, no difference was found as well between malignant cysts and pseudocysts based on size ( $P = 0.53$ ). Malignant cysts include 4 mucinous cystic neoplasms, one intraductal papillary mucinous cyst of side-branch variety, and one cystic degeneration of pancreatic adenocarcinoma.

**Conclusion:** Cyst size has significant variation. Radiographic prediction of cyst malignancy cannot be reliably made on size alone. Pseudocysts, benign cysts, and malignant cysts have no significant differences in size.

**Metastatic Cholangiocarcinoma Masquerading as Mesenteric Ischemia**

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**Purpose:** Perihilar Cholangiocarcinoma represents 60–80% of cholangiocarcinomas. Obstructive jaundice is the presentation in 90% of patients. Other symptoms include weight loss, anorexia, acholic stools, fatigue and abdominal pain.

**Methods:** 60 year old male presented with postprandial abdominal pain, sitophobia and 30 lb weight loss over 2 months. The pain was constant periumbilical worsened with eating. Abdomen was tender without peritoneal findings. With mesenteric ischemia in the differential a CT was performed. Mesenteric vessels were patent but small bowel and colon were diffusely thickened and mild left intrahepatic ductal dilation was noted. Surgical evaluation and review of CT suggested mesenteric ischemia was less likely. Enteroscopy and colonoscopy with ileoscopy and biopsies were negative. Liver enzymes were normal except alkaline phosphatase 185, AST 52 and ALT 104. ERCP to evaluate biliary dilation revealed mild narrowing of medial branch of right intrahepatic and tight stricture at take off of left intrahepatic. Stent was placed across the stricture. Brushings were negative. Cholangiocarcinoma was suspected when the CA 19–9 of 2000 U/mL returned in conjunction with the ERCP findings. Although CT scan did not suggest metastatic disease a CT PET scan demonstrated metastasis to the right lobe, peritoneum, mesentery and bowel. Biopsy of porta hepatitis using biliary stent as landmark was consistent with adenocarcinoma of pancreatic or biliary origin (CK19 +). The patient opted for hospice care succumbing 2 months later.

**Results:** Perihilar Cholangiocarcinoma typically presents with obstructive jaundice. This patient presented with abdominal pain, sitophobia and weight loss, more consistent with mesenteric ischemia. Despite normal bilirubin, evaluation of intrahepatic duct dilation with CA 19–9, cholangiography and biopsy was needed for diagnosis. CT PET imaging accurately staged disease where CT failed. In elderly patients with negative work up for mesenteric ischemia biliary dilation should be investigated. Cholangiocarcinoma with metastasis to bowel and peritoneum can present with pain similar to mesenteric ischemia from meal stimulated increase in bile flow and/or obstruction.[figure1]

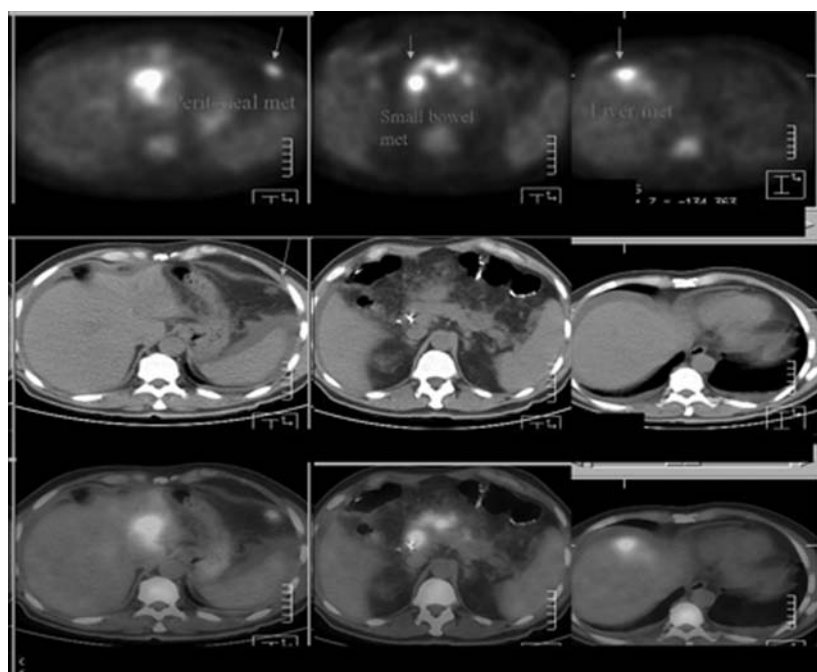
**Predictors of Morbidity from Local Complications in Severe Acute Pancreatitis**

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**Purpose:** Severe Acute Pancreatitis (SAP) is often complicated by necrosis, pancreatic duct disruption and fluid collections. These local complications (LC) cause significant morbidity and often require repeated interventional procedures.

**Methods:** Multiple approaches employed to retrospectively identify patients with SAP presenting to Mayo Medical Center (MMC) within the first week of onset of pancreatitis included review of: a) CT reports for the term “pancreatic necrosis”, b) medical ICU data base, and c) global EMR for Jan. 2002–Dec. 2006. All pts. had at least one of the following indicators of SAP: (1) Pancreatic necrosis on dynamic CT, (2) APACHE II score  $\geq 8$ , (3) Late development of LC such as pseudocyst or abscess, (4) prolonged ICU admission due to AP, and (5) Length of hosp.stay (LOS)  $\geq 10$  days. Pt. medical records were reviewed for demographics, etiology of SAP, BMI, pertinent lab values and clinical course with particular attention to the eventual need for interventional Rx of LC. The two groups, SAP with and without LC, were compared with regards to demographics, lab markers and clinical outcomes.

**Results:** Eighty-four pts. presented with SAP within 1 week of onset between Jan. 2002 and Dec. 2006. Among them, 56% (47/84) developed LC and 37% (31/84) required radiologic (N = 13), endoscopic (17) and/or surgical (11) intervention for the complication. The mean age of the 47 pts. who developed LC was 55.1 yrs., vs. 56.9 yrs in pts with SAP but no complications; 66% (31/47) of pts with LC were male, vs. 73% (27/37) of patients with no complications (both  $P = NS$ ). The mean BMI was 30 for both groups. The mean LOS was 35.4 d. for pts. with subsequent local complications compared to 9.2 d. for pts. without complications ( $P = < .0001$ ). The mean admission WBC, hematocrit, and serum creatinine for pts. with complications were 36.3, 38.9, and 1.5, compared to 16.4, 41.1, and 1.2 in pts. without complications (all  $P = NS$ ). The mean peak amylase and lipase levels for



pts. with and without complications were 1230 and 4196 vs 950 and 3190 ( $P$  values NS).

**Conclusion:** Our data showed no correlation between age, gender, BMI, admission WBC, hematocrit, serum creatinine, or peak pancreatic enzymes levels and development of local complications secondary to severe acute pancreatitis. Local complications of SAP can incur significant prolongations in hospital stay.

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### Long-Term Follow-Up of Endoscopic Papillary Balloon Dilation Compared to Endoscopic Sphincterotomy for the Extraction of Bile Duct Stones

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**Purpose:** Endoscopic papillary balloon dilation (ED) for the extraction of bile duct stones is proposed to prevent late-occurring complications compared to endoscopic sphincterotomy (ES). In our previous multi-center study, 237 patients were randomized to have ED or ES. 30 day morbidity occurred in 18% (7% severe, 2 deaths) of ED and 3% (0 severe) of ES patients ( $P < 0.001$ ) and the study was terminated at the 1st interim analysis. Our purpose is to determine the long-term outcomes of ED vs. ES in the same cohort.

**Methods:** Standardized telephone interviews and medical records review regarding morbidity beyond 30 days was performed by blinded personnel not involved in clinical management. Complications were stratified by consensus criteria. Patients crossed over from ED to ES were analyzed as ES.

**Results:** To date, 131 (55%) participants have been located and 34 (14%) are known dead. With a mean follow up of 9.7 (8.3–11.0) years, 63 (48%) ED and 68 (52%) ES participants have been located. 18 (14%) ED and 16 (12%) ES patients have died, but the causes are known in only 6 and none were pancreatobiliary-related. Reliable data are available on 97 (41%; 70 women, 27 men) with a mean age of 44 (26–95) years and the treatment groups are evenly matched. Results are shown in the table. A multivariate regression analysis was performed on age, gender, cholecystectomy status and periampullary diverticulum, and none of these factors significantly contributed to complications in either treatment group.

	Long-Term Complications		
	ED N = 63	ES N = 68	$P$
Patients with any complications	18 (29%)	14 (21%)	$P = 0.31$
Events			
Abdominal pain	15 (24%)	13 (19%)	$P = 0.53$
Jaundice	2 (3%)	3 (4%)	$P = 0.52$
ERCP	3 (5%)	4 (6%)	$P = 1.0$
Recurrent stones	0	3 (4%)	$P = 0.25$

**Conclusion:** 1. Long-term complications of ED and ES occur at similar rates. 2. These findings do not support ED as preferential treatment for bile duct stones to prevent long-term complications of ES.

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### Management of Acute Cholangitis with Periapillary Diverticula – Is Endoscopic Sphincterotomy Really Effective for Recurrence Prevention?

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**Purpose:** This is an overview on management of acute cholangitis with periampullary diverticula at Okinawa Chubu Hospital, an educational medical care institute with 550 beds.

**Methods:** We reviewed all cases from 7/2003 to 12/2006 (41 months) in which patients underwent therapeutic endoscopic retrograde cholangiopancreatogram (therapeutic ERCP). We compared the treatment outcome of acute cholangitis cases between those with periampullary diverticulum and without periampullary diverticulum. Statistical analysis was performed using chi-square test.

**Results:** There were 636 cases of therapeutic ERCP in 41 months at our institute. Of these, 57 cases of acute cholangitis with periampullary diverticula and 90 cases without periampullary diverticula were noted. No significant difference in sex, age, common bile duct diameter or status post cholecystectomy were noted between the two groups. 5 cases (8.8%) of recurrence in the group with acute cholangitis with periampullary diverticula and 9 cases (10%) of recurrence in the group without periampullary diverticula (N.S.) were noted. 4 of 5 (80%) recurrent acute cholangitis with periampullary diverticula and 18 of 57 (31.6%) non recurrent acute cholangitis with periampullary diverticula were noted ( $P = 0.03$ ).

**Conclusion:** There were no significant risk for acute cholangitis in a patient with periampullary diverticula compared with a patient without periampullary diverticula.

For an acute cholangitis patient with periampullary diverticula, management with sole endoscopic sphincterotomy (ES) was not effective in preventing future recurrent acute cholangitis. Combination of bile duct stenting or endoscopic retrograde bile duct drainage (ERBD) before or along with ES were effective.

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### Inferior Vena Cava Compression Due to Biloma: A Case Report

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**Purpose:** Biloma is an uncommon but well known complication of cholecystectomy. It varies in sizes from very small inconsequential leaks to very large collections causing pressure symptoms such as in gastric outlet obstruction. However, biloma causing inferior vena cava compression leading to significant edema has not been reported so far.

**Case Report:** We report the case of a 55 year old female presenting with abdominal distention and lower extremity edema, a month after an open cholecystectomy. Physical examination showed distended abdomen with hepatomegaly and pitting edema of bilateral lower extremities. Laboratory data revealed normal hepatic function test except for an elevated alkaline phosphatase. Contrast enhanced computed axial tomography scan (CAT scan) of the abdomen revealed a 15 cm × 20 cm fluid collection (open arrows) displacing the liver far to the left and compressing on the inferior vena cava (closed arrows). The diagnosis of biloma was established at percutaneous drainage with resolution and relief of her symptoms.

**Discussion:** Biloma is a localized collection of bile usually from iatrogenic injury. Laparoscopic cholecystectomy is the most common cause of bile duct injury leading to biloma formation although it can also occur spontaneously when gall stones are impacted in the bile ducts leading to disruption. The incidence varies from 0–7%. Other causes include local infection, cholangiocarcinoma, transarterial chemoembolization of hepatic malignancy and endoscopic retrograde cholangiopancreatography. Postoperative biloma commonly manifests within one week after surgery characterized by abdominal pain, fever, vomiting and jaundice. CAT scan and magnetic resonance imaging are superior to ultrasonography. Continuity between fluid collection and biliary tree can be determined by radionuclide cholescintigraphy. Chemical analysis of the aspirate can confirm the diagnosis. Percutaneous drainage is the treatment of choice for large collections otherwise endoscopic sphincterotomy with or without stent placement is usually adequate. Occasionally surgery may be needed for a persistent biloma particularly if infection ensues.[figure1]



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#### A Comparison of Ranson's Criteria Versus Sequential Organ Failure Assessment Score (SOFA) in Predicting Intensive Care Unit Admission, Morbidity and Mortality in Acute Pancreatitis in the Emergency Room

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**Purpose:** To evaluate the outcome of patients admitted with acute pancreatitis and a comparison of Ranson's score with maximum Sequential Organ Failure Assessment (SOFA) score to predict the prognosis in the emergency room.

**Methods:** Data from consecutive patients admitted with acute pancreatitis in a referral center in the year 2001–2006 were retrospectively collected. All charts were reviewed for Ranson's score at admission and 48 hrs and SOFA score daily for the first 5 days. The total maximum SOFA score was calculated summing the highest scores for all six systems. Organ dysfunction was considered as SOFA score of 1 or 2 points and organ failure as a SOFA score of 3 or more. The primary outcomes were mortality, admission to the intensive care unit and duration of hospital stay. Patients with <18 years of age, known diagnosis of chronic pancreatitis or serum amylase and lipase < 3 times normal were excluded.

**Results:** 167 patients were admitted to the hospital with a diagnosis of acute pancreatitis over the 2 year period (90 male, 77 female; median age 52 years, range 18–96 years). The etiology of pancreatitis was alcohol (42, 25%), gall stone (68, 40%), post-ERCP (9, 5%) or other (48, 30%). The Ranson's score at admission was  $1.26 \pm 1.07$ . The maximum SOFA score at admission was  $1.64 \pm 1.76$ . 32 (19%) patients needed admission to the ICU. 7 patients died from complications of acute pancreatitis. The median hospital stay for all patients was 7 days (2–50 days). There was no association between Ranson score on admission and mortality. However, patients with a SOFA score  $\geq 3$  were 5.9 times more likely to die. (95% CI: 1.1 – 31.4), than those with a score < 3. 52.6% of those with Ranson  $\geq 3$  are admitted to the ICU during their hospitalization, whereas 16.3% of those with Ranson < 3 are admitted to the ICU,  $P < 0.001$ . 40.4% of those with SOFA  $\geq 3$  are admitted to the ICU during their hospitalization, whereas 10.9% of those with SOFA < 3 are admitted to the ICU,  $P < 0.0001$ . An elevated Ranson Score ( $P < .02$ ) or SOFA score ( $P < .001$ ) on admission was predictive of a length of stay greater than 7 days.

**Conclusion:** On admission, both Ranson's score and SOFA score are useful in predicting the duration of hospital stay. The SOFA score was better in predicting the overall mortality.

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#### Clinicopathologic Features of Surgically Resected Pancreatic Cystic Lesions

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**Purpose:** Pancreatic cysts represent varying degrees of malignant potential. Because of the limited ability to predict the precise nature of these lesions, surgical resection is often advised. The aim of this study was to identify clinicopathologic features that correlate with malignant potential of surgically resected pancreatic cysts.

**Methods:** Using available Gastrointestinal Pathology and Surgical Oncology databases, we retrospectively reviewed all surgical resections of pancreatic cysts performed at The Mount Sinai Hospital from August 1995 to June 2006. We recorded patient characteristics, presenting symptoms, and preoperative imaging. Among a total of 74 patients, the medical records of 63 patients were available. Cysts were categorized as benign (N = 35), premalignant (N = 22), or malignant (N = 17).

**Results:** Benign, premalignant, and malignant cysts occurred in 47.3%, 29.7%, 23.0% of resected lesions, respectively. After excluding pseudocysts, we found that patients with premalignant/malignant pancreatic cysts were more likely to be older and to demonstrate pancreatic duct dilatation on pre-operative imaging. Malignant cysts were significantly more likely to be associated with jaundice, to occur in the head or neck of the pancreas, and to have ductal dilatation on preoperative imaging (Table 1). Malignant cysts also demonstrated a trend toward increased likelihood of being symptomatic ( $P < 0.1$ ).

**Conclusion:** In this retrospective study, nearly half of pancreatic cyst resections were performed for benign entities. Ductal dilation occurred more commonly in premalignant and malignant cysts. Malignant cysts were associated with clinical symptoms, jaundice, and location in the head/neck. These factors may provide physicians with an improved ability to discriminate between benign, premalignant, and malignant pancreatic cysts. Using a newly established Pancreatic Neoplasia Database, we hope ultimately to better identify appropriate patients for surgical resection for pancreatic cystic lesions.

**Table 1.** Comparison of Nonmalignant and Malignant Pancreatic Cysts

	Nonmalignant (N = 48)	Malignant (N = 17)	P value
Presence of Symptoms	41%	82.4%	$P = 0.089$
Presence of Jaundice	0%	17.6%	0.009
Ductal Dilatation	21.4%	63.6%	0.012
Location in Head/Neck	28.9%	75.0%	0.005

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#### Lack of Corellation between Liver Enzymes and the Presence of a Bile Leak Following Laparoscopic Cholecystectomy

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**Purpose:** Biliary tract leak following laparoscopic cholecystectomy occurs in approximately 1–5% of all patients. Most bile leaks are restricted to the gall bladder bed and perihepatic region; retained calculi may or may not be present, causing potential elevations in liver function tests (LFTs). Common

symptoms indicating bile leak are abdominal pain, vomiting, and abdominal distension. Many surgeons routinely obtain LFTs after all laparoscopic cholecystectomies, but it is unclear whether liver enzyme elevation is a predictor of bile leak following lap chole. The purpose of this study was to determine if routine postoperative LFTs can predict a post operative bile leak.

**Methods:** All patients diagnosed as having ERCP documented postoperative bile leak from April 2003 to May 2007 were identified. Preoperative and post operative liver enzymes and patient symptoms were obtained through chart review and retrospective analysis.

**Results:** Bile leak was observed in 25 patients (0.9%). Among the 25 patients found to have a bile leak, 9 (36%) had post operative evidence of elevations of AST, ALT, or Alk Phos (greater than  $1.5 \times$  normal). Only 6 (24%) had post operative fever and 5 (20%) leukocytosis. All patients (100%) had evidence of post operative abdominal pain, nausea or both. There was a statistically significant difference in pre- and postoperative alanine aminotransferase and alkaline phosphatase (39 vs 66 U/L;  $P = 0.01$  and 96 vs 133 U/L;  $P = 0.05$ , respectively).

**Conclusion:** There was no correlation with liver enzyme elevation and presence of bile leak, with only 36% of patients with bile leak manifesting  $1.5 \times$  elevations in Alk Phos, ALT or AST. Postoperative elevations in liver function tests are frequently seen after laparoscopic cholecystectomy; however, these elevations do not predict bile leak following laparoscopic cholecystectomy. LFTs should be obtained only when clinically indicated.

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### Groove Pancreatitis: A Case Report To Illustrate a Little-Known Entity

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**Purpose:** Groove pancreatitis is a segmental type of chronic pancreatitis that involves the pancreatoduodenal groove. Recognition of this entity in the differential diagnosis of pancreatic cancer may avert the extensive and morbid surgery that is performed to treat pancreatic malignancy.

We present a case report of a 41 year old male with a history of alcohol dependence who presented with 2 days history of post-prandial abdominal pain that was relieved by vomiting (sometimes self-induced). His sitophobia led to a 20 lb weight loss in 2 months. He admitted 2 days of coffee ground emesis and melena prior to admission. He denied use of NSAIDs. His father had developed pancreatic cancer at age 50.

He was not anemic on admission, had normal liver function tests and only mildly elevated lipase and amylase. An abdominal CT with IV contrast revealed a circumscribed hypodense solid mass, 5 cm  $\times$  5 cm, that appeared to arise within the duodenal wall and was located in the duodenal sweep displacing the pancreatic head and causing apparent gastric outlet obstruction. Extracorporeal ultrasound showed no mass or pseudocyst of the pancreas. EGD showed a subtotal and impassable postbulbar duodenal stenosis due to erythematous, edematous polypoid mucosa with surface ulceration. Biopsies revealed a lymphoplasmacytic infiltrate confined to the lamina propria with eosinophils, marked edema and villous blunting.

The patient was managed conservatively and was discharged in 8 days tolerating a regular diet. A repeat CT after 1 month showed less distension of the duodenum and an irregular soft tissue density in the head of the pancreas suggestive of pancreatitis. Follow-up EGD showed improvement of the esophagitis and duodenal wall erythema. Repeat biopsies were negative for dysplasia or malignancy.

Groove pancreatitis affects the pancreatoduodenal groove. This potential space is prone to the collection of pancreatic secretions, leading to inflammation and marked cicatrization in this area. This results classically in duodenal stenosis.

The pathogenesis is unclear but may involve protein plugs or occlusive tumors in the duct of Santorini, cystic dystrophy of the duodenal wall developing in a heterotopic pancreas, gastric surgery, peptic ulcer or even dysfunction

of the minor papilla, either primarily or secondary to local inflammatory or neoplastic processes. Dilation and stenting of the accessory duct has resulted in the full resolution of groove pancreatitis.

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### Comparison of Cyst Fluid DNA Analysis Utilizing Two Different DNA Interpretations

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**Purpose:** While the utility of a variety of molecular and biochemical markers in fluid from pancreatic lesions have been reported, the 'ideal' marker remains unknown. A panel of molecular tests is now commercially available for DNA analysis from cyst fluid (RedPath laboratory, Pittsburgh, PA). In a small series reported in a previous abstract, we found poor correlation between the commercial test interpretation and the results of cytology and surgical pathology. Recently, the result of the PANDA study (GIE 2007; 65:AB101) was reported classifying cysts as nonmucinous, nonmalignant mucinous and malignant mucinous based on 4 criteria provided by RedPath. This study was conducted to correlate the results of the criteria used in the PANDA study in interpreting the results of the molecular analysis with the final diagnosis in our previous series as confirmed by cytology and/or surgical pathology.

**Methods:** In our small series we identify 12 patients in whom a definitive diagnosis was made by surgical pathology (8) or cytology (4) from a series of 154 patients evaluated by EUS-FNA for the presence of cystic pancreatic lesions. In these patients we reviewed the detailed results of following: The presence of k-ras mutation, number of mutations, DNA amount (Optical Density = OD), DNA quality (Cyclic Threshold). In the PANDA study OD > 10 and CT < 27 with high amplitude mutations are found to be most consistent with malignant mucinous cysts.

**Results:** Of the 12 patients in the study k-ras mutation was found in 5 patients, 4 with mucinous lesions and one with neuroendocrine tumor; 4 other patients with mucinous lesion had no k-ras mutation. Six patients had elevated amount (OD > 10) of good quality DNA (CD < 27.2), of these 4 had malignant mucinous lesions, one had benign MCA on surgical pathology, and one had pseudocyst. Three patients with malignant mucinous lesions had elevated DNA amount, but had low quality DNA (CD > 27). The two patients with neuroendocrine tumors had low amount of poor quality DNA.

**Conclusion:** The final pathology results of this small series seem to correlate better with the criteria of the PANDA study than with the commercial interpretation. Their criteria seem to demonstrate greater specificity for the type of the cyst, whether it is nonmucinous, nonmalignant mucinous or malignant mucinous, but seem to still lack significant sensitivity. The pattern we saw in the NE tumors needs to be further studied.

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### Epigastric Pain with Very High LFTs and Pancreatic Enzymes – An Unusual Presentation of Papillary Stenosis

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**Purpose:** The typical case of papillary stenosis is described as middle aged female who presents with recurrent episodes of right upper abdominal pain occurring several years after cholecystectomy with mild elevations of LFTs. Here we report an unusual case of papillary stenosis who presented with acute pancreatitis like symptoms with very high levels of LFTs and amylase and lipase followed by rapid improvement.

**Methods:** A 53-year-old white female s/p cholecystectomy came to the emergency department because of epigastric pain, nausea and vomiting for 2 days. On physical exam, she had epigastric tenderness but no jaundice or dehydration. The liver enzymes were grossly elevated, with an aspartate aminotransferase (AST) level of 2006 IU/L, an alanine aminotransferase (ALT) level of 1359 IU/L, and an alkaline phosphatase (ALP) value of 180

IU/L. Total and direct bilirubin levels were 2.2 mg/dL and 1.3 mg/dL respectively. Serum amylase and lipase were 1536 U/L and 1915 U/L respectively. A CT scan of abdomen and pelvis and abdominal sonogram were negative for pancreatitis or stones in the pancreato-biliary tree. ERCP revealed a normal papilla. Cholangiogram showed a dilated common hepatic duct of 8 mm with benign tapering to the ampulla. The cystic duct joined the common hepatic duct only few millimeters away from the ampulla. Hence the patient had a very small common bile duct. No stones were noted in the biliary tree. With the elevated LFTs, biliary pain and dilated duct, this was a case of type 1 papillary stenosis. Sphincterotomy was performed. Post ERCP follow up labs showed a marked decline in LFTs and amylase and lipase and there was marked improvement in abdominal pain. At follow up visit one week after sphincterotomy, the patient remained completely asymptomatic and the LFTs and amylase and lipase were almost completely normalized (AST = 33, ALT = 154, ALP = 195, amylase = 101, lipase = 46 and total bilirubin = 0.3).

**Conclusion:** Papillary stenosis is not a common condition and often presents diagnostic dilemma to the clinicians. An ERCP with sphincterotomy is instrumental in diagnosing and treating papillary stenosis, and should be considered in postcholecystectomy cases with abdominal pain and elevated LFTs. Endoscopic sphincterotomy is a recommended treatment for papillary stenosis (type 1 SOD) and is very effective and safe in experienced hands.

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### Prophylactic Antibiotics in Necrotizing Pancreatitis: A Meta-Analysis

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**Purpose:** Acute necrotizing pancreatitis is associated with substantial morbidity and mortality. Prophylactic antibiotics have been used in these patients to decrease potential infection in an effort to decrease mortality. However, multiple randomized controlled trials (RCTs) on the subject have shown mixed results. Based upon these inconsistencies, we conducted a meta-analysis to analyze the effects of prophylactic antibiotics in necrotizing pancreatitis.

**Methods:** MEDLINE, Cochrane Central Register of Controlled Trials & Database of Systematic Reviews, PubMed, and recent abstracts from major conference proceedings were searched (May 2007). RCTs comparing prophylactic IV antibiotics to no prophylactic antibiotics in the setting of necrotizing pancreatitis were included. Standard forms were used to extract data by two independent reviewers. The effects of prophylactic antibiotics were analyzed by calculating pooled estimates of mortality, infected pancreatic necrosis, length of hospital stay, non-pancreatic infections, and surgical intervention. Separate analyses were performed for each outcome by using odds ratio (OR) or weighted mean difference (WMD). Heterogeneity was assessed by calculating the  $I^2$  measure of inconsistency. Publication bias was assessed by Harbord-Egger, Begg-Mazumdar, and funnel plot methods.

**Results:** Seven studies (N = 429) which met the inclusion criteria were included in this analysis. Prophylactic antibiotics for acute necrotizing pancreatitis significantly decreased the length of hospital stay (WMD -5.64, 95% CI: -11.01 - -0.27,  $P = 0.04$ ) and the rate of non-pancreatic infections (OR 0.55, 95% CI: 0.34-0.88,  $P = 0.01$ ). No significant differences between the prophylactic antibiotic and the control groups were noted for mortality (OR 0.71, 95% CI: 0.41-1.23,  $P = 0.22$ ), infected necrosis (OR 0.72, 95% CI: 0.45-1.16,  $P = 0.18$ ), and surgical intervention (OR 0.82, 95% CI: 0.52-1.30,  $P = 0.40$ ). Heterogeneity was not statistically significant for any variable ( $P > 0.05$ ). No significant publication bias was noted.

**Conclusion:** Prophylactic antibiotics in necrotizing pancreatitis significantly reduced the length of hospital stay and rate of non-pancreatic infections. However, no significant differences were found for mortality, infected necrosis, and need for surgical intervention. Prophylactic antibiotics in necrotizing pancreatitis have a limited role in decreasing length of stay and other non-pancreatic infections.

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### Adenocarcinoma of the Pancreas Presenting as Diabetic Ketoacidosis

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**Purpose:** Adenocarcinoma of the pancreas (ACP) is often advanced at presentation and carries a poor prognosis. Infrequently, it presents as diabetes mellitus (DM.) ACP presenting as diabetic ketoacidosis (DKA) is vanishingly rare.

**Methods:** A 50-year old Caucasian woman presented to hospital after ten days of progressive nausea, vomiting, anorexia and fatigue. She was known to have essential hypertension and major depression, but had no history of DM. In the emergency department the patient was found to have: glucose 898 mg/dL, anion gap 19, bicarbonate 17 mmol/L, beta-hydroxybutyrate 3.7 mmol/L and both glucosuria and ketonuria. The patient was diagnosed with DKA and treated with fluid, insulin and potassium. Shortly thereafter the patient complained of epigastric pain. An abdominal ultrasound revealed mild dilatation of the common bile duct, signs suggestive of acute cholecystitis and a suspicious liver nodule. Further history uncovered a sixty pound weight loss over the preceding six months. The previously normal liver indices increased over three days as follows: AST 974 u/L, ALT 425 u/L, total bilirubin 1.8 mg/dL to a peak of 9 mg/dL. Amylase and lipase remained normal throughout. A CT scan of the abdomen showed a mass in the head and uncinate process of the pancreas, dilatation of the intra- and extra- hepatic bile ducts and secondary pancreatitis with atrophic changes. On MRI the mass was found to encase the Superior Mesenteric Artery. Endoscopic ultrasound revealed invasion of the Portal Vein. Tissue biopsy of the head of the pancreas diagnosed the lesion as an adenocarcinoma of the pancreas of intermediate grade. The cancer was stage IV at diagnosis and was not amenable to curative surgical intervention. The disease continued to progress despite radiation therapy and systemic chemotherapy with gemcitabine and temozolomide. The patient decided to discontinue aggressive treatment and pursue hospice care.

**Results:** This case demonstrates that sinister etiologies may underlie DM or DKA that present in mid to late adulthood. Glucagonomas occasionally present with DKA, whereas a presentation of ACP with DKA is exceedingly uncommon. Malignancy is an important etiology and early diagnosis is imperative for successful curative surgical intervention.

**Conclusion:** Both DKA and DM of late onset in the context of even moderate weight loss should prompt an evaluation for pancreatic disease.

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### Admission Apache II for Prediction of In-Hospital Mortality in Acute Pancreatitis

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**Purpose:** To determine the accuracy of the admission APACHE II score for prediction of in-hospital mortality in acute pancreatitis (AP) using population-based data. In addition, to determine thresholds for increased mortality by APACHE II score.

**Methods:** Patient data was generated from the Cardinal Health Research Database, a large population dataset that has supported publicly reported hospital performance in Pennsylvania for 20 years. All cases from Jan 2004-Dec 2004 identified by principal diagnosis ICD9-CM 577.0 (AP) were included. Admission APACHE II scores were calculated for all patients. Missing values were entered as normal. Performance of admission APACHE II was measured using area under the ROC curve (AUC). Comparison of APACHE II score with observed mortality was performed to determine appropriate cutoffs for high vs. low-risk patient groups.

**Results:** There were 18,256 cases from 212 hospitals with 225 deaths (1.2%). Mean age was 55.0 and 49.3% were males. Mean admission APACHE II

score was 7.0 among all patients. Using our method, admission APACHE II AUC = .828. Observed mortality by Apache II score is depicted in the table below.

**Conclusion:** Our application of the APACHE II scoring system produced an accurate tool for early prediction of mortality in patients with AP. Mortality in our AP population did not significantly increase until an APACHE II score >10.

Observed Mortality by APACHE II score

APACHE II score	Observed Mortality (%)
≤10	<1%
11–15	2.75%
16–20	11.0%
>21	32.5%

Overall Mortality = 1.2%

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### Septic Pylephlebitis Mimicking Acute Biliary Obstruction

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**Purpose:** Portal and mesenteric vein thrombosis are uncommon. It has been associated with hypercoagulable state, oral contraceptive use, pregnancy and septic pylephlebitis. We present a case of septic pylephlebitis mimicking acute biliary obstruction.

**Case Report:** 68 year old male presented with fever, chills, left lower quadrant abdominal pain, leukocytosis and obstructive biliary picture. There was no ascites. His work up was negative for cholecystitis, cholangitis and hepatitis. Further work up revealed *E. coli* bacteremia. Contrast enhanced Computed Tomography (CECT) (Fig. 1) showed sigmoid diverticulitis with thrombus in the inferior mesenteric vein and the portal vein. Hypercoagulable work up was negative. The patient was treated with piperacillin-tazobactam and full anticoagulation with warfarin. The patient clinically improved, liver profile studies normalized and serial CECT (Fig. 2) showed resolution of the thrombus.

**Discussion:** Septic pylephlebitis is difficult to clinically diagnose. The fact that our patient had abdominal pain with *E. coli* bacteremia necessitated CECT of the abdomen and pelvis which revealed inferior mesenteric and portal vein thrombosis. Condat et al. (1) has reported eight in a series of 33 patients with portal vein or mesenteric thrombosis directly linked to abdominal sepsis including diverticulitis (N = 2), bacteroides bacteremia (N = 1) cholangitis (N = 3), hepatic abscess (N = 1) and appendicitis with peritonitis (N = 1). There were no other identifiable risk factors for hypercoagulable state. Doppler ultrasound and CECT can be used when the diagnosis is suspected (1). CECT has an advantage in that it is not operator dependent. In Condat et al series, early anticoagulation lead to 31% of patients achieving complete thrombus resolution and 46% achieving partial thrombus resolution. Our patient had partial thrombus resolution within 30 days of the diagnosis. These findings are also comparable to the literature (2, 3). Furthermore, occurrence or recurrence of intestinal infarction was not commonly observed on anticoagulation therapy (1, 2, 3). In addition, treatment of the infectious focus and antibiotics is necessary for optimal outcome. Antibiotics are recommended for 4–6 weeks in most cases (4). Our patient received antibiotic therapy for four weeks.

**Conclusion:** Septic pylephlebitis should be considered when bacteremia with an intestinal bacterial species coincides with mesenteric or portal vein thrombosis. Early anticoagulation is vital for good outcome.

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### Early Oral Feeding in Mild Acute Pancreatitis: A Randomized Prospective Trial

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**Purpose:** One of the pillars of managing patients with acute pancreatitis has been the concept of “placing the pancreas at rest”. At admission, patients are typically not allowed to take any food or fluids orally (NPO) while provided intravenous hydration. Several prospective trials have shown that early nasojejunal, and more recently, nasogastric feeding is safe and beneficial. When compared to parenteral nutrition, there is a consensus among the trials demonstrating that enteral nutrition results in decreased infectious complications, decreased length of stay (LOS) and significant cost savings. Unfortunately, nasojejunal feeding often requires endoscopic or radiologic placement of tubes. Nasogastric feeding is uncomfortable and may pose an increased risk for aspiration.

**Methods:** In order to determine the safety of early oral feeding in patients with acute pancreatitis, a randomized prospective study was performed. A consecutive series of patients with mild acute pancreatitis were invited to participate (Ranson Score of less than 3, and an APACHE Score less than 6, and with no evidence of organ dysfunction or pancreatic necrosis). After informed consent was obtained, patients were randomized to one of three groups. Group 1 was placed NPO, standard of care, until pain resolved and amylase fell below 3 times normal. Group 2 was placed on a semi-elemental formula as tolerated starting within 12 hours of admission. Group 3 was allowed to consume a regular diet as desired starting within 12 hours of admission. Patients were followed for pain medication requirements, complications, length of stay, and recurrence of disease.

**Results:** To date, 33 patients have been enrolled in the study. Mean age  $52 \pm 13$ , 12 male, 11 female. The three groups of patients did not differ regarding age, gender and etiology of acute pancreatitis. There were no differences in narcotic usage, complications and LOS among the three groups of patients. Morphine use was  $6.1 \text{ mg} \pm 2.8 \text{ mg}$  per day for the first 3 days in Group 1,  $5.5 \pm 3.1 \text{ mg}$  day in Group 2 and  $6.5 \pm 2.8 \text{ mg}$  per day in Group 3. The mean length of stay was  $4.2 \pm 1.1$  days,  $3.8 \pm 2.5$  days and  $4.1 \pm 1.7$  days, respectively.

**Conclusion:** We conclude that patients with mild acute pancreatitis can safely be fed a regular diet as tolerated. This study provides further evidence that “placing the pancreas at rest” is not necessary in the management of patients with acute pancreatitis.

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### Ethanol Pancreatic Injection of Cysts: Results of a Prospective Multicenter, Randomized, Double Blinded Study

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**Purpose:** Pancreatic cystic lesions (PCL) often represent a form of early malignancy (mucinous cystic lesions).

**Purpose:** To determine the safety and effectiveness of Endoscopic Ultrasound (EUS)-guided ethanol lavage of PCLs.

**Hypothesis:** The rate of cyst ablation as a result of ethanol (EUS-ETOH lavage with 80% ethanol) will be greater than the rate achieved with saline (EUS-SL lavage).

**Methods:** This was a prospective, randomized, controlled trial that enrolled patients with a PCL 1–5 cm (0–4 septations). After first lavage, all patients were offered a second lavage with ethanol. CT was repeated 3 months after the last EUS. Surgical resection was permitted at any time. The PCLs were assigned a diagnostic category based upon cytology, cyst fluid CEA and/or surgery.

**Results:** From 10/04–6/07, 54 patients were consented, 12 were excluded prior to initial lavage and 42 (26 F; mean age:69 yrs) with suspected benign mucinous (35) or nonmucinous pancreatic cystic tumors (4) and pseudocysts (3) were randomized to EUS-ETOH (25) or EUS-SL (17). Cyst size: median



19 mm (range: 10–40) and location: head/uncinate (18), body (16) or tail (8). The change in the size (surface area) and rate of ablation are shown in Table 1.

**Findings:** EUS-Ethanol resulted in a significant decrease in cyst size as compared to saline lavage. 10/23 (43%) subjects had complete ablation of the PCL as determined by imaging; all as a result of ethanol lavage. Complications from EUS-ETOH: there were two episodes of acute pancreatitis. Results of surgical pathology in 3 subjects who underwent PCL resection after lavage: 1) benign 3.5 cm IPMN-50–75% epithelial ablation (ETOH); 2) benign 2.2 cm mucinous cyst with histology demonstrating 100% epithelial ablation, (ETOH); 3) 1.5 cm benign mucinous cyst with intact epithelium (Saline).

**Conclusion:** EUS-ETOH decreased pancreatic cyst size and resulted in an ablation rate greater than that achieved with EUS-Saline.

EUS Lavage (s)	Baseline cyst surface area (mean + SEM)	Post procedure cyst surface area (mean + SEM)	Complete cyst ablation rate (EUS or CT scan)	Complications of EUS lavage (pancreatitis)
Saline N = 15	1.7 cm <sup>2</sup> + 0.9	1.4 cm <sup>2</sup> + 0.6	0/15	0
Ethanol (one) N = 36	1.5 cm <sup>2</sup> + 0.3	1.1 cm <sup>2</sup> + 0.3*	2/37	1
Ethanol (two) N = 23	1.4 cm <sup>2</sup> + 0.4	1.0 cm <sup>2</sup> + 0.4**	10/23	1

\*P = .002 \*\*P = .0001 ETOH vs Saline

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### Comparison of MRCP with the Gold Standard, ERCP, for Evaluation of the Hepatobiliary Tract in a Large Urban Community Hospital

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**Purpose:** Endoscopic retrograde cholangiography (ERCP) is the gold standard in imaging the hepatobiliary tract (HBT). Recent studies have compared findings from magnetic resonance cholangiography (MRCP) with findings from ERCP for HBT imaging. Most studies were reported from large academic tertiary care centers. The purpose of this study is to identify the utility of MRCP for imaging the HBT in a large urban community teaching hospital that relies on ERCP.

**Methods:** This is a retrospective chart review which included all inpatients and outpatients who had both MRCP and ERCP between August 1, 2006 and March 31, 2007. Referring physicians included private community physicians and full time hospital staff physicians. For inclusion, both ERCP and MRCP had to be: 1) completed within a 2 week period, and 2) ordered to visualize the HBT. A Chi-Squared test of independence was used to examine the concordance of abnormal and normal findings from MRCP and ERCP. We determined sensitivity and specificity from MRCP findings compared to results from ERCP (the gold standard).

**Results:** Fifty-two joint MRCP and ERCP studies were completed in 48 patients (32 women and 16 men; age range 24 to 89 years). In 52 joint studies, ERCP was abnormal in 48 (92%) of the cases, while MRCP was abnormal in 42 (81%). Among 6 cases with normal MRCP in which there was an abnormal ERCP, the abnormalities included identification of a stricture of the HBT in 5 cases. Using ERCP as the gold standard, MRCP had a calculated sensitivity of 83% with a calculated specificity of 50%. Examination of the concordance of abnormal and normal findings from MRCP and ERCP did not identify a significant difference (Chi-squared 2x2 contingency table: P = 0.08).

**Conclusion:** It is unclear whether results from large academic tertiary care centers can be applied to community hospitals. In contrast to published studies, our findings suggest that MRCP may miss a significant abnormality in 11% of cases. In addition, there was a strong trend (P = 0.08) toward an increase in the number of cases with abnormal ERCP compared to the number of cases with abnormal MRCP. ERCP appeared to be a better test for detecting strictures in imaging of the HBT. In a large community hospital, MRCP may be an acceptable imaging modality in patients in whom a stricture of the HBT is less likely.

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### Failure of Antibiotics To Prevent Infection in Patients with Necrotizing Pancreatitis: A Meta-Analysis

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**Purpose:** Bacterial infection has been a major cause of morbidity and mortality in patients with acute pancreatitis. Multiple prospective studies have evaluated antibiotics in the prevention of infection of pancreatic necrosis in patients with severe acute pancreatitis. The studies have shown conflicting results. In order to better understand the role of antibiotics in the prevention of infectious complications in patients with necrotizing pancreatitis, the following meta-analysis was performed.

**Methods:** A Medline search was performed to identify all trials evaluating the efficacy of antibiotic prophylaxis in the treatment of patient with necrotizing pancreatitis. Studies included in the final analysis were (1) full length papers published in peer reviewed journals, (2) included only patients with necrotizing pancreatitis, (4) prospective, (5) placebo-controlled, and (6) defined outcome as sepsis, infection of pancreatic necrosis and mortality. Studies were combined and scored. A pooled analysis of the overall rates of pancreatic infection, sepsis and mortality was calculated. A weighted mean was utilized. The 95% confidence intervals were calculated for the placebo and treatment arms. In the analysis, the absolute risk reduction (ARR) and relative risk reduction (RRR) were calculated.

**Results:** Seven randomized, prospective, placebo controlled studies were identified. Two were double blinded. A total of 455 patients were included in the analysis, 228 patients given prophylactic antibiotics and 227 patients given placebo. In combining the studies, using a weighted mean meta-analysis, there was no significant benefit in using prophylactic antibiotics compared to placebo in the prevention of pancreatic infection, sepsis and mortality.

**Conclusion:** Although earlier studies had suggested that antibiotic prophylaxis can prevent infectious complications in patients with necrotizing pancreatitis, this meta-analysis, which includes the more recent double-blinded trials, shows no benefit. The results of this study are consistent with current guidelines of the American College of Gastroenterology: "prophylactic antibiotics are not recommended in patients with necrotizing pancreatitis".

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### Prevalence of the Calcium Sensing Receptor (CaSR) Gene Polymorphisms in Patients with Recurrent Acute and Chronic Pancreatitis with or without SPINK1 N34S

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Carolina, Charlestown, PA; Department of Medicine, University of Michigan Medical Center, Ann Arbor, MI and Department of Medicine, Evanston Northwestern Healthcare, Evanston, IL.

**Purpose:** The calcium sensing receptor (*CaSR*) plays an important role in calcium homeostasis. It is expressed in pancreatic acinar and ductal cells, as well as in the cells of the parathyroid gland and kidney tubule. The *CaSR* 1011 C>G single nucleotide polymorphism (SNP) is associated with slightly elevated serum calcium levels in general population. Felderbauer et al. (*Scand Journal of Gastroenterology*, 2006; 41: 343–348) reported three novel *CASR* gene mutations in a cohort of 19 families with idiopathic chronic pancreatitis and suggested that *CaSR* gene might be a co-factor with *SPINK1*-mutations in a complex pancreatitis risk model. To test the hypothesis that the *CASR* polymorphisms alter the risk of *SPINK1* N34S subjects for recurrent acute (RAP) and chronic pancreatitis (CP).

**Methods:** 65 affected subjects with idiopathic and familial pancreatitis and 58 controls were selected, of these 38 patients and 11 controls had *SPINK1* N34S polymorphism. The *CaSR* gene exon 2, 3, 4 and 7, which contains most of the known functional polymorphisms, were sequenced. Based on initial results, three nonsynonymous SNPs in exon 7 were genotyped in an additional 77 affected subjects and 176 controls.

**Results:** The 3 novel *CaSR* SNPs (F391F, E790E, and R896H) previously reported by Felderbauer et al were not identified in our population. In the exon7 *CaSR* 1011 C/G SNP the G allele was more common in *SPINK1* N34S subjects (8 of 36, 22%) than either pancreatic patients without *SPINK1* N34S (8 of 104, 8%,  $P = 0.034$ ), or controls (16 of 234, 7%,  $P = 0.012$ ). None of the 11 control subjects with *SPINK1* N34S had *CaSR* 1011 G allele. The other two common *CaSR* SNP in exon7 were not associated with pancreatitis.

**Conclusion:** The *CaSR* 1011 G allele alone is not a susceptibility factor for RAP or CP. However, in the presence of *SPINK1* N34S, the *CaSR* 1011 G allele increases the susceptibility to idiopathic RAP and CP. These data support a complex genetic model of pancreatitis susceptibility.

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### Efficacy and Safety of a Fully Covered Self Expandable Metal Stents (CSEMS) for Distal Biliary Neoplasia: Preliminary Data of a Multicenter Study

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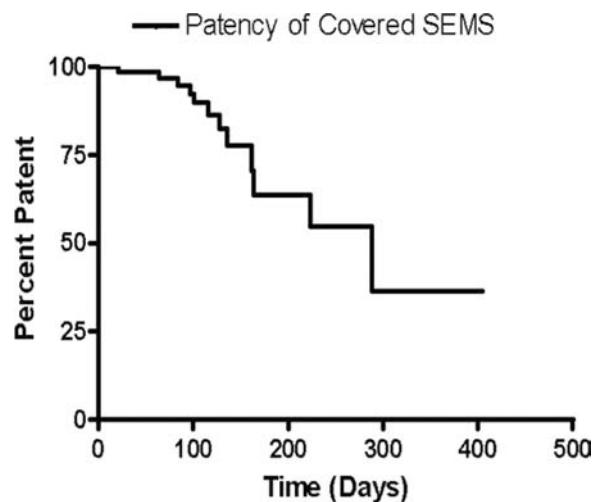
**Purpose:** Partially covered self-expandable metal stents have not clearly been shown to be superior to uncovered stents in terms of long term patency. Fully covered metal stents may provide longer patency, but possibly have a higher rate of complications including stent migration and cholecystitis. We conducted this multicenter study to analyze the efficacy and complication rates of fully covered SEMS (CSEMS) in malignant biliary obstruction.

**Methods:** Between October 2003 and May 2007, 87 Patients (50 males, 66 ± 15 y/o) underwent ERCP with placement of a 10 × 40, 60, 80 or 100 mm CSEMS (VIABIL®, Conmed) for the palliation of distal biliary neoplasia. Survival, stent patency, complications, and causes of stent dysfunction were analyzed prospectively. All but 7 patients underwent biliary sphincterotomy before stent placement.

**Results:** At the end of the study period, 48 patients were alive and 3 were lost of follow-up. Twelve CSEMS malfunctioned; 1 migrated and 11 occluded (10 related to biliary debris and 1 to tumor overgrowth). CSEMS were left in place and remained patent for a mean of 98 ± 76 days (range: 1–406). Patency at 90, 180 and 360 days were respectively 90, 64 and 36% (see Figure). Complications included a self limited wire perforation, 2 post ERCP

pancreatitis and 2 cholecystitis. Six patients underwent curative resection. Nine patients had their stent removed and replaced in a single session (6 for tissue sampling, 1 for pancreatic drainage, 2 for occlusion).

**Conclusion:** Fully CSEMS have acceptable patency rate with minimal short term complications. Decreased long term patency appears related mainly to biliary debris. Further long term data is required to confirm this observation.[figure1]



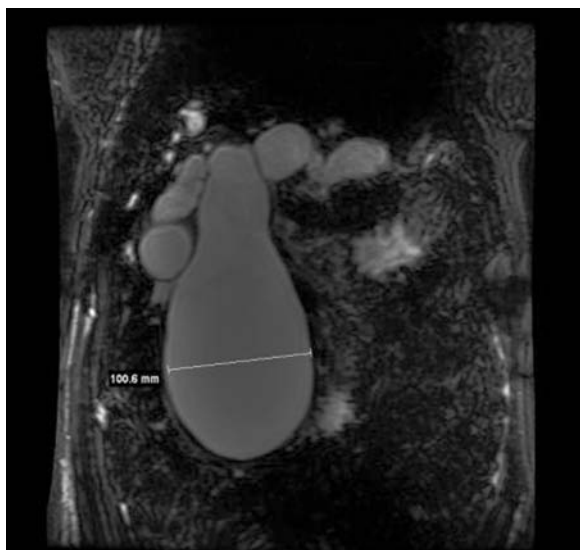
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### A Patient with Choledochal Cyst

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**Purpose:** A 29 year old Hispanic woman presented to the ER with complaint of intermittent right upper quadrant pain of 8 month duration. The pain started when she was 1 month pregnant, was achy in character and associated with nausea and vomiting. After she delivered her baby, she noticed yellowish discoloration of her eyes. She complained of pruritus and anorexia but denied any fever, chills, diarrhea, or loss of weight. She did not have any significant medical illnesses and was not taking any chronic medications at home. She denied smoking, alcohol or drug abuse. Family history was noncontributory. On physical examination, eyes were icteric and right upper quadrant was tender. Laboratory evaluation showed total bilirubin of 6 mg/dL, direct bilirubin of 5.2 mg/dL, elevated transaminases (AST-140 IU/L, ALT-126 IU/L) and elevated alkaline phosphatase (459 IU/L). CT scan of the abdomen showed severe intra and extrahepatic biliary ductal dilatation and a 10.2×11.7 cm cyst that was compressing and displacing the pancreatic head, duodenum and inferior vena cava. MRCP showed significant intra and extrahepatic biliary ductal dilatation with common bile duct massively distended to 10 cm size. A diagnosis of choledochal cyst was made.

Choledochal or biliary cysts are cystic dilatations, which may occur singly or in multiples throughout the bile ducts. They are presumed to be multifactorial in etiology. An abnormal pancreaticobiliary junction is present in about 70 percent of patients. Choledochal cysts may be complicated by cholelithiasis, choledocholithiasis, cystolithiasis, pancreatitis, intrahepatic abscess, biliary cirrhosis and malignancy particularly cholangiocarcinoma. The treatment of choice is complete excision of the cyst with construction of a biliary-enteric anastomosis.[figure1][figure2]



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### Recurrent Acute Pancreatitis Leads to Chronic Pancreatitis: A Prospective Case Series

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**Purpose:** Growing evidence suggests that recurrent acute pancreatitis (AP) leads to chronic pancreatitis (CP), but this sequence is seldom demonstrated in human subjects. The Sentinel Acute Pancreatitis Event (SAPE) hypothesis supports that an initial episode of AP is the first step in a complicated series of events which ultimately leads to CP.

The aim of this study is to identify patients who evolved from recurrent AP (RAP) to CP.

**Methods:** The Severity of Acute Pancreatitis Study (SAPS) database was reviewed. Patients with their first episode of AP were prospectively followed.

**Results:** Three of 102 enrolled AP patients fulfilled the above sequence of events. All 3 patients were teenagers. Upon initial presentation, there was

no evidence of CP on the CT scan performed and no clear AP etiology was identified. Patients were completely asymptomatic between recurrent attacks. All patients progressed to CP, as evidenced by CT and ERCP findings, over a relatively short period of time (Table 1). Two patients were positive for SPINK-1 mutations (N34S), and subsequently underwent total pancreatectomy with pancreatic islet autotransplantation with good results.

**Conclusion:** The three patients presented here seem to fulfill the SAPE hypothesis. Their clinical course supports the concept that pancreatitis may be a syndrome with a broad spectrum of severity ranging from an isolated episode of AP to CP. Further studies and the development of additional disease models are needed in order to fully establish this link.

Patients Characteristics			
	Patient A	Patient B	Patient C
Age at first attack (years)	13	16	13
Gender	F	M	M
Presumed etiology	Idiopathic	Idiopathic	Idiopathic
Family History of pancreatitis	Brother with RAP	None	None
AP attacks per year	4	6	5
Time interval between initial attack of AP and development of CP (years)	1.5	3	3.5
Genetic Testing	PRSS1 -/-, SPINK1 +/-, CFTR -/-	PRSS1 -/-, SPINK1 +/-, CFTR -/-	PRSS1 -/-, SPINK1 -/-, CFTR -/-
Follow up	s/p total pancreatectomy and pancreatic islet cell auto-transplantation	s/p total pancreatectomy and pancreatic islet cell auto-transplantation	Enzyme replacement and pain medications

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### Cluster of Cases of Gallstone Complications in Patients Less Than 31 Years of Age at UMC, Fresno, CA

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**Purpose:** In the U.S., it is unusual to see gallstone-related complications in patients below the age of 31 except in Pima Indians and patients with hemolytic conditions. At the University Medical Center in Fresno, CA, we have encountered a large cluster of young patients with complications of gallstones. The nationwide prevalence of gallstones in patients below the age of 31 is only about 5%. A study was undertaken to further evaluate this young age group of patients who underwent cholecystectomy.

**Methods:** The medical records department compiled a list of patients from January 2004 to August 2006 who had cholecystectomy. The charts of patients under age 31 at the time of the cholecystectomy were reviewed retrospectively. Data collected included age, ethnicity, body mass index, predominant complications due to gallstones, and the type of stone found at the time of surgery. Predisposing factors, including indirect hyperbilirubinemia and DM, were also assessed.

**Results:** A total of 1,370 patients had undergone cholecystectomy for gallstones in the study period. 370 patients (27%) were below the age of 31. The medical charts of these 370 patients were reviewed. Cholesterol stones represented 57.79%, brown stones about 11.92%, green stones 6.42%, and pigment stones 3.66%. The rest were of undetermined type. About 89.90% of patients were Hispanic, 7.33% were Caucasian, and all other races constituted about 2.75% of the study population. The average BMI was 31.75, and the average age was 24.31. Non-Hispanic patients below the age of 31 accounted for more than 20% of the cholecystectomy cases. None of the

patients had evidence of a hemolytic condition, and only eight cases were associated with diabetes.

**Conclusion:** Of all patients undergoing cholecystectomy at our institution in Fresno, CA from 2004 to August 2006, an unusually high percentage (27%) were below the age of 31. The fact that the study population was predominantly Hispanic does not entirely explain this institutional phenomenon, because though the Hispanic population is known to have a higher prevalence of cholelithiasis, the shift to a younger age group for cholecystectomy has not been reported in the U.S. to our knowledge. This shift to the younger age group for cholecystectomy affected both the Hispanic and the non-Hispanic patient population, thus raising the possibility of local factors. These findings may require further investigation to determine the etiology of cholelithiasis in this geographic population.

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### A Retrospective Comparison of ERCP Complications with Conventional ERCP vs. Wire Guided ERCP

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**Purpose:** Endoscopic Retrograde Cholangiopancreatography (ERCP) is an invasive endoscopic technique which affords both diagnostic studies and therapeutic interventions. This procedure is associated with potentially severe complications including post ERCP pancreatitis. A factor that may increase the risk of post ERCP pancreatitis is contrast opacification of the pancreatic duct. Recently, a wire guided technique has been developed which avoids opacification of the pancreatic duct. The purpose of this study was to determine whether there was any difference in post ERCP pancreatitis requiring hospitalization when conventional cannulation using contrast is compared with wire guided cannulation.

**Methods:** A retrospective review of ERCP at a single institution was performed. In 2005 there was a change made from a conventional contrast injection approach to use of a wire guided approach to ERCP. This latter technique involves cannulating the common bile duct with a guide wire prior to injecting contrast. If the pancreatic duct is cannulated, no contrast is injected. A retrospective chart review of ERCPs performed in April through September 2004 and January through June 2005 was performed. Data on procedure length, indication, and complications including pancreatitis was gathered. Pancreatitis was defined as pain post procedure associated with an increased lipase and requiring a hospital stay.

**Results:** A total of 282 ERCPs were performed within the study period by 3 endoscopists, with 14 episodes of post-ERCP pancreatitis (5.0%) documented. The mean age of the patients was 63 years with 42% being male. The major indications for ERCP were biliary colic or obstructive jaundice (75%) and therapeutic intervention was performed in 77% of cases. There were no differences in demographics between groups.

In the 2005 period, 130 ERCPs were performed, with 3 cases of pancreatitis, compared with 152 ERCPs in 2004, with 11 cases of pancreatitis [Odds Ratio 0.30 (0.08 to 1.11)]. During the study period, 167 ERCPs were performed using the wire guided technique, with 4 cases of pancreatitis, compared with 115 ERCPs performed conventionally, with 10 cases of pancreatitis [Odds Ratio 0.26 (0.09 to 0.79)]. Procedure length was a mean of 32 min and 35 min for conventional and wire guided ERCP respectively. ( $P = 0.08$ ).

**Conclusion:** This retrospective study demonstrates that wire guided ERCP is associated with a lower rate of post-ERCP pancreatitis than conventional ERCP.

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### Efficacy and Safety of ERCP in the Pediatric Population When Performed by Adult Gastroenterologists: A 6 Year Review

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**Purpose:** The aim of this study is to evaluate the outcomes of ERCP in the pediatric population when performed by adult gastroenterologists. Previous studies have shown that ERCP in the pediatric population is both efficacious and safe. Little information is available on the safety and efficacy of ERCP on the pediatric population when performed by an adult gastroenterologist.

**Methods:** A retrospective chart review was performed at a single academic center of all 25 patients under the age of 18 that underwent ERCP by an adult trained endoscopist from 2000–2006. Demographic data was recorded including age, sex and ethnicity. Clinical data collected included significant medical history including BMI, clinical indications for ERCP, therapy during ERCP (such as sphincterotomy, pancreatic or biliary stent placement and biliary stone extraction), immediate post ERCP complications and hospital length of stay. BMI was recorded as well.

**Results:** 25 ERCPs were performed, on patients 18 years of age and younger from 2000–2006. Of which, 13 were female and 12 were male with an average age of 13.3 and an age range of 8–18 years old. Significant medical history included hemoglobinopathies like Sickle Cell Disease ( $N = 2$ ) and Spherocytosis ( $N = 1$ ), PSC ( $N = 1$ ), IBD ( $N = 1$ ) and Obesity ( $N = 5$ ). Average BMI was 17.37. Average hospital length of stay was 4.8 days with a range of 0–10 days. Primary indications for ERCP were Cholangitis ( $N = 2$ ), Dilated Common Bile Duct ( $N = 9$ ), Biliary/Pancreatic stent removal ( $N = 2$ ), Suspected Choledochal Cyst ( $N = 1$ ), Recurrent Pancreatitis ( $N = 4$ ), Pancreatic Pseudocyst ( $N = 1$ ) and Abnormal Intraoperative Cholangiogram ( $N = 6$ ). Sphincterotomy was performed on 19 patients and the common bile duct was successfully cannulated 96% of the time (22 of 23 cases). CBD stones were extracted 100% of the time (15 of 15 cases) while pancreatic/bile duct stents were deployed successfully in 2 of 2 cases. No deaths were observed. One patient had a post ERCP papillotomy bleed after a needle knife was used to open a choledocoele. This was attributed to a hematologic disorder (Von Willenbrand Disease). One patient with choledocholithiasis who underwent ERCP with sphincterotomy and biliary stone extraction had a mild post ERCP Pancreatitis. No perforations were observed.

**Conclusion:** In this study, ERCP appears to be a safe and effective procedure in the pediatric population when performed by an adult trained endoscopist.

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### Painless Jaundice and an Extremely Elevated CA 19-9 Secondary to Choledocholithiasis, Not Malignancy

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**Purpose:** Painless jaundice and CA 19-9 levels in the tens of thousands has been suggested to equate to malignancy with nearly 100% probability. Here we report a case of a 55 yr-old alcoholic male presenting with painless jaundice and a CA 19-9 of 62,000 IU/L which normalizes after removal of a large CBD stone.

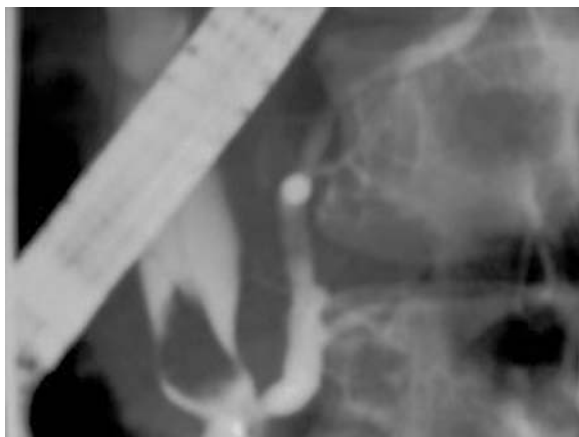
**Methods:** A 55-yr-old hispanic male with an admitted history of heavy alcohol use presented with jaundice that was recognized by friends over a 2 week period with no complaint of abdominal pain or fever. He stated he had a decreased appetite for several days and a subjective history of weight loss, but other than the jaundice had no other symptoms. The results of the physical examination were unremarkable except for icteric skin and sclera. Laboratory data on showed a leukocytosis of 23 UL; normal Hgb and Plt. The bilirubin level was 22.6 mg/dL with a direct of 21.4 mg/dL. Alkaline phosphatase 293 IU/L; AST 62 mg/dL; ALT 166 mg/dL. Amylase and Lipase were normal. His CA 19-9 was found to be 62,500 IU/L with a CEA and CA 125 within normal limits.

CT scan of the abdomen showed intra/extra hepatic ductal dilatation with CBD to 1.6 cm near the pancreatic head. Normal pancreatic duct and no appreciable mass. An ERCP was performed which showed a large mobile filling defect in the mid CBD. An extraction of a 2 cm stone was performed.

**Results:** Follow up studies 3 weeks post extraction showed a normalization of all liver function tests, negative ANA, ASMA, and AMA; as well as a

normalization of the CA 19-9 to 18 IU/L. All biliary pathology specimens were negative for malignancy.

**Conclusion:** CA 19-9 is a glycoprotein synthesized by normal pancreatic, biliary, gastric, colonic, endometrial, and salivary epithelial cells. It has "tumor association" but is not a specific tumor marker. Reports estimate that CA 19-9 has a sensitivity of 80–90% for pancreatic cancer and 60–70% for biliary cancer. Non-cancerous lesions such as cholangitis, cholestasis, and pancreatitis can be associated with elevated CA 19-9 levels, but are thought to be uncommon higher than 1000 IU/L. Thus, an elevated CA 19-9, even with high clinical suspicion for malignancy is not always malignancy.[figure1]



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### Selected Diagnostic and Therapeutic ERCP and EUS Cases Can Be Safely and Effectively Performed in an Ambulatory Surgery Center Setting

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**Purpose:** To evaluate the feasibility and safety of performing endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic ultrasonography (EUS) in a free-standing Ambulatory Surgery Center.

**Methods:** The first sixteen outpatients undergoing ERCP and/or EUS procedures in an ambulatory surgery center were evaluated and analyzed for the purposes of this study. A detailed chart review, phone interview and follow-up with the treating physicians and the patients to evaluate outcome, satisfaction and record complications was completed. Equipment and materials from Olympus Corporation (endoscopes, endosonographic probes, processors, catheters and sphincterotomes), Microvasive (catheters, sphincterotomes, balloons, plastic stents) and ERBE (Argon plasma coagulator power unit and peripherals) were used.

**Results:** Sixteen (N = 16) patients (3 M/13 F, age range: 24–94) underwent ERCP and/or EUS for a variety of indications. All patients were ambulatory and had an ASA classification < III. ERCPs were performed in 15 patients and EUS in 3 (2 patients had a diagnostic EUS followed by therapeutic ERCP). Three (3) patients underwent only diagnostic ERCP, eleven (11) patients had ERCP with sphincterotomy and stone extraction, two (2) patients required plastic stent placement, one (1) patient had ampullectomy following stent placement and one (1) patient underwent EUS with FNA of pancreatic mass and adjacent lymph node. Common bile duct cannulation rate was 100% (one patient required pre-cut sphincterotomy). Procedure time ranged from 18 to 73 min. All patients were observed and discharged within 3 hrs. Complications included one patient with post-ERCP pancreatitis treated conservatively with pain medications and bowel rest and one patient with an intravenous site/skin complication. No patient required transfer or admission to the hospital. Patient satisfaction rates were very high.

**Conclusion:** Diagnostic and therapeutic ERCP and EUS procedures can be safely and effectively performed in carefully selected patients in an Ambulatory Surgery Center.

## 221

### Endoscopic Drainage of Pancreatic Fluid Collections Using Fully Covered Metallic Stents (CSEMS): A Feasibility Study

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**Purpose:** Endoscopic drainage of pancreatic fluid collections (PFC) has been proven to be effective, however, the conventional technique of using plastic double pigtailed may require multiple sessions for effective drainage. Fully covered metallic stents (CSEMS) offer the option of providing a larger diameter access fistula for drainage and might increase the final success rate.

**Methods:** Between January 2007 and May 2007, 14 patients (56 ± 5 y/o, 9 male) underwent placement of CSEMS (VIABIL®, Conmed) for the drainage of PFC. Three patients were drained endoscopically and 11 required EUS-guided drainage. A double pigtail was placed along side (6 cases) or into the CSEMS (8 cases) to prevent migration. Etiology, indications for drainage, pseudocyst size, sessions required, complications, follow-up and final results were prospectively recorded (see table).

**Results:** Etiology of PFC was gallstone (9), alcohol (3) and other (2). Mean size was 10 ± 5 cm. A median of 1 session was required to achieve drainage. Mean time of follow-up until final evaluation was 75 ± 46 days (range 15–180). Complications included, superinfection (4), and bleeding from a pseudoaneurysm (1). One patient experienced migration of the CSEMS with resolution of the collection. A total of 13/14 (93%) patients responded successfully.

**Conclusion:** CSEMS seem to offer an efficient and safe alternative for the drainage of pancreatic fluid collections. A prospective and randomized study should be performed comparing this technique to conventional drainage with plastic pigtailed.

Details of Cases Drained with CSEMS

Case	Indication	Size	Sessions	Complication	Results
1	GOO	8	1	None	Success
2	Infection	12	1	None	Success
3	Infection	15	2	Superinfection	Success
4	Infection	13	2	Superinfection	Success
5	Pain	12	4	Superinfection	Success
6	Infection	5	1	Bleeding	Success
7	Infection	7	1	Migration	Success
8	Infection	8	1	None	Success
9	Pain	17	4	Superinfection	Failure
10	Infection	9	1	None	Success
11	Infection	9	1	None	Success
12	Infection	11	1	None	Success
13	Pain	5	1	None	Success
14	Infection	5	1	None	Success

GOO: Gastric outlet obstruction

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### A Single Institution's Initial Experience with Spyglass™ in the Diagnosis and Management of Biliary Disease during ERCP

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**Purpose:** To evaluate the clinical utility, safety and ease of use of Spyglass™ (a single-operator peroral cholangiopancreatography system) during endoscopic retrograde cholangiopancreatography (ERCP).

**Methods:** A retrospective chart review was performed of the ERCP cases during which Spyglass™ was used. For each case, the following outcomes were assessed: success of introducing the device into the bile duct; successful identification of filling defects; use and success of electrohydraulic lithotripsy (if performed); use and success of directly visualized forceps biopsies; and yield of biopsies.

**Results:** Spyglass™ cholangiopancreatography was attempted in 6 patients. A single operator performed each case. Indications for Spyglass™ included: unexplained abdominal pain of suspected biliary origin (N = 1) and filling defects seen on initial cholangiogram [suspected choledocolithiasis (N = 3) and malignant stricture (N = 2)]. Cannulation with Spyglass™ was successful in 5 of 6 patients (83.3%). The single failed cannulation was due to difficult anatomy from a suspected malignant biliary stricture in the distal common bile duct. Identification of filling defects was achieved in 4 of the 5 successful cannulations (3 with stones, 1 with malignancy). Biopsies were performed in 1 case with a successful diagnosis of a ductal carcinoma. Therapy using electrohydraulic lithotripsy (EHL) via the Spyglass™ device was attempted in 2 patients (1 with a common bile duct stone, 1 with a cystic duct stone). Partial clearance was achieved in each case. Failure of successful lithotripsy was due to (1) the size of the common bile duct stone and (2) inability to maintain good stone to EHL probe contact in the cystic duct. No procedure related complications occurred.

**Conclusion:** In this small retrospective review, the Spyglass system demonstrated adequate visualization of the biliary tree to facilitate the diagnosis of biliary strictures and lithotripsy of large CBD stones during ERCP. Further investigation to identify the optimum patient characteristics for cholangiopancreatography with this system is required and ongoing.

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**Multiple Biliary Stent Placement Using Conventional Long Wire (OASIS) and Short Wire (Fusion OASIS with IDR) Stenting Systems for Benign Bile Duct Strictures (BBDS) – A Retrospective Study**  
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**Purpose:** Multiple biliary stenting is technically challenging. This retrospective analysis compared outcomes (success and complication) of conventional long wire (OASIS, Cook) with short wire (Fusion OASIS with intraductal release, Cook) stenting systems in multiple stenting for BBDS.

**Methods:** We reviewed the GI Trac (electronic record system) and hospital electronic record/imaging as well as patient followup records to identify patients with BBDS who had undergone multiple stenting, initially with the OASIS and subsequently Fusion OASIS systems. Sludge/stones formed above the stricture were removed with basket prior to stent replacement. Total number of stents, time (minutes) taken and post ERCP pancreatitis were documented for each ERCP procedure. Data are expressed as (mean ± SD) and analyzed with Student t-test.

**Results:** 8 patients underwent a total of 60 stenting procedures between 2000 and 2006, 35 using OASIS and 25 using Fusion OASIS system. There was a statistically significant difference in number of stents per procedure ( $1.63 \pm 0.731$  versus  $2.36 \pm 0.569$ , respectively,  $P < 0.0001$ ). The time required for first stent placement was  $38 \pm 19.1$  and  $46.5 \pm 16.2$  minutes respectively ( $P < 0.14$ ). Mean time for subsequent stents was  $7.3 \pm 5.29$  and  $5.95 \pm 3.05$  minutes respectively ( $P < 0.2$ ). No post-ERCP pancreatitis was observed in any patients.

**Conclusion:** More time is spent on subsequent ERCP's in removing sludge/stones that formed above the stricture prior to stent deployment. Intraductal release (IDR) of guide wire obviates the need for repeat cannulation and negotiation of the stricture and facilitates multiple stent placement for BBDS. A prospective trial is needed to confirm the efficacy.

## Results of multiple stenting

	OASIS	Fusion OASIS	P*
# Patients	35	25	
Stent /ERCP (mean + SD)	$1.63 \pm 0.731$	$2.36 \pm 0.569$	$<0.0001$
Time (minutes) first stent	$38 \pm 19.1$	$46.5 \pm 16.2$	$<0.14$
Time (minutes) subsequent stents	$7.3 \pm 5.29$	$5.95 \pm 3.05$	$<0.2$
Post ERCP pancreatitis	0	0	

\* Student t-test

## 224

### Hemoconcentration Alone Is an Unreliable Predictor of Mortality in Acute Pancreatitis

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**Purpose:** To examine whether hemoconcentration (HC) at admission predicts in-hospital mortality in acute pancreatitis (AP). To determine whether a new definition of intravascular volume depletion [Hgb + BUN] is a better predictor for in-hospital mortality.

**Methods:** Patient data was generated from the Cardinal Health Research Database, a large population dataset. All cases from Jan 2004–Dec 2004 with principal diagnosis ICD9-CM 577.0 (AP) were included. Two cohorts of patients were identified: transferred vs. non-transferred pts. HC was defined as elevated hgb > 14.6 g/dL (hct 44%). The combination of elevated hgb > 14.6 g/dL and BUN > 25 mg/dL (Hgb + BUN) was used as a marker for intravascular volume depletion. Comparison was made between HC and our newly defined marker of intravascular volume depletion for prediction of in-hospital mortality in the two cohorts.

**Results:** There were a total of 202 transferred and 17,852 non-transferred cases of AP. Overall mortality was 5.5% vs 1.2% in transferred vs. non-transferred pts respectively ( $P < 0.001 \chi^2$ ). HC was a significant risk factor for mortality only among transferred pts. Combined (Hgb + BUN) was a significant predictor of mortality in both cohorts. Admission intravascular volume depletion as assessed by our new criteria was significantly more common among transferred vs non-transferred pts. (9.4% vs. 2.8%,  $P < 0.001 \chi^2$ ).

**Conclusion:** Hemoconcentration alone is an unreliable predictor of mortality in AP. Hgb + BUN was a more robust predictor of mortality for both transferred and non-transferred pts. These findings help explain discordant results from previous studies of hemoconcentration in AP.

Mortality Comparisons				
	Transferred (overall mortality 5.5%)		Non-Transferred (overall mortality 1.2%)	
	% Mortality	OR [95% CI]	% Mortality	OR [95% CI]
HC	11.1%	7.44 [1.56, 35.4]	1.26%	1.05 [0.78, 1.41]
Hgb + BUN	26.3%	10.5 [2.86, 38.9]	5.59%	5.31 [3.51, 8.02]

HC = hemoconcentration, Hgb+BUN = (hgb > 14.6 g/dL + BUN > 25 mg/dL)

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### Utility of the SPYGLASS Cholangiopancreatography (SCPS): An Initial Series of 26 Cases at a Tertiary Care Center

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**Purpose:** The SCPS is a recent innovation in which a single endoscopist is able to perform cholangiopancreatography. The clinical utility of this new device has not been well studied. The goal of our study was to review our initial experience with the SCPS and assess its usefulness as a diagnostic and therapeutic tool.

**Methods:** We retrospectively examined 26 cases using SPCS. All procedures were performed by one of three biliary endoscopist with experience in cholangioscopy. Success in imaging the desired ductal structures, in performing electrohydraulic lithotripsy (EHL), and in guiding biopsy was assessed.

**Results:** In 20 cases cholangioscopy utilized the Spyscope catheter and in 6 cases the SPYGLASS video fiber was passed through a triple lumen sphincterotome. The common duct (CBD) was examined in 25 cases and the pancreatic duct (PD) in 1. In 13 cases (group 1) the SCPS was used to evaluate potentially malignant strictures. There were 4 cases (group 2) where the SCPS was used for EHL of large CBD stones. In 9 cases (group 3) the SCPS was used in the diagnostic evaluation of various findings in the CBD or PD.

In group 1 the Spyscope catheter was successfully used in 9/13 cases and the fiber/sphincterotome was used in 5/13 cases to visualize cbd strictures. Tissue was obtained in all pts by standard forceps, brushing, or the miniature Spy forceps (5/13 cases) and was diagnostic of malignancy in 4/13 pts. Spy forceps provided sufficient tissue in 4/5 biopsies, with 2 demonstrating malignancy.

In group 2 stones were visualized well and good placement of the EHL probe occurred in all cases. Stone pulverization only occurred in 1/3 patients (1/4 cases).

In group 3 the Spyscope catheter was used in 7/9 cases and the fiber/sphincterotome in 2/9 cases. Examination ruled out stone, mass or stricture in 7/9 cases. Directed wire guided cannulation of an intrahepatic duct was performed in one case. A choledochal cyst was successfully sampled with Spy forceps in one case. SPCS examination was found to be clinically useful in all pts in group 3.

**Conclusion:** Our initial use of the SCPS proved successful in evaluating complex biliary and pancreatic issues. Excellent visualization was achieved in all cases. SPCS added to our ability to biopsy malignant strictures, though the yield was lower than expected in this early experience. EHL was technically facilitated though two cases of very hard stones proved recalcitrant. SPCS was found to be clinically useful in the majority of cases.

## SMALL INTESTINE/UNCLASSIFIED

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### Psychological Correlates of Gluten-Free Diet Adherence in Adults with Celiac Disease

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**Purpose:** To determine what set of personality/psychological characteristics are related GFD adherence in an adult population diagnosed with celiac disease while further examining the role of depression and anxiety in relation to adherence with the GFD

**Methods:** 157 adults with biopsy-confirmed CD on the GFD for > 3 months completed surveys of depression, anxiety, personality characteristics, self-efficacy and self-reported GFD adherence, provided a blood sample, and participated in an evaluation of GFD adherence conducted by an expert dietician.

**Results:** Significant correlations were found between bloodwork, self-reported, and expert evaluation. Logistic regression results indicated that the following variables were independently associated with GFD adherence: conscientiousness ( $B = -.04$ ,  $S.E. = .01$ ,  $P < .00$ ), values ( $B = -.10$ ,  $S.E. = .05$ ,  $P < .05$ ), other food intolerances (odds ratio = .28, 95% CI .10-.78),

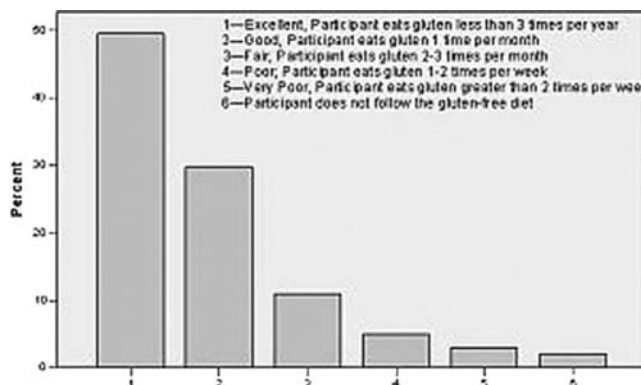
and symptoms ( $B = .05$ ,  $S.E. = .02$ ,  $P < .03$ ). A regression model was built from these significant associations. The resulting model effectively predicted whether a participant was compliant or non-compliant based on significant psychological and demographic/disease-specific factors. Successful prediction rates of GFD adherence for the final model was 75.8% for those rated to be adherent with the GFD and 54.5% for those rated to be non-adherent with the GFD.

**Conclusion:** The model of psychological and demographic/disease-specific characteristics developed can be used to identify patients who may be at greater risk for poor dietary adherence in order to provide additional support, education and encouragement.

Regression Model of Variables Associated With GFD Adherence

	B or Odds Ratio (P-value)
Values Trait	-.10 (0.05)
Conscientiousness	-.04 (0.003)
Symptom Severity	-.05 (0.03)
Food Intolerances	OR .28 (95% CI 0.10-.78)

[figure 1]



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### A Prospective Study of Factors Associated with Increased Gluten-Free Diet Adherence in Adults with Celiac Disease

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**Purpose:** In recent years increasing number of individuals have been diagnosed with celiac disease (CD). The only treatment for CD is lifelong adherence to a strict gluten-free diet (GFD). Despite its efficacy, adherence to the GFD is poor and factors which influence this are poorly understood. We sought to determine which factors influence GFD adherence in adults with CD.

**Methods:** A survey of items determined to be important in GFD adherence was developed by an expert committee and focus groups of patients with CD. The survey was administered to 154 adults with biopsy proven celiac disease who then underwent blood testing for IgA tissue transglutaminase (tTG) levels and a standardized GFD evaluation by a nutritionist skilled in CD. Univariate and multivariate analysis were conducted to determine factors associated with adherence level.

**Results:** In the study population, GFD adherence was high with 44.2% following a strict gluten free diet. Gender, Age at participation, age at diagnosis of CD, length of time on GFD, marital status, educational achievement, and employment status were not correlated with level of adherence. Factors associated with GFD adherence are listed in the table below.

**Conclusion:** A number of factors were found to be correlated with GFD adherence, including cost, ability to follow the diet outside the home, membership in a celiac disease advocacy group, belief in the importance of following the GFD, and the ability to follow the GFD despite changes in mood and stress. These results provide a foundation for the design of educational interventions that may be used to target individuals at high risk for non-adherence to the GFD.

Factors Associated with GFD adherence

Factor	P Multivariate*
Cost makes GFD adherence difficult	0.011
Concern with purposeful gluten exposure	0.001
Concern with accidental gluten exposure	<0.001
Understanding of GFD	0.002
Ability to follow GFD when traveling	0.012
Ability to follow GFD when dining out	<0.001
Ability to follow GFD during social events	0.007
Membership in CD advocacy group	0.008
Comfort following GFD at work	0.003
Belief that avoiding gluten is important for health	0.027
Mood/stress do not affect GFD adherence	0.008
Presence of other food intolerances	0.023

\*Controlling for age, gender, education, age of diagnosis and marital status

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### A Prospective Study of Five Measures of Gluten Free Diet Adherence in Adults with Celiac Disease

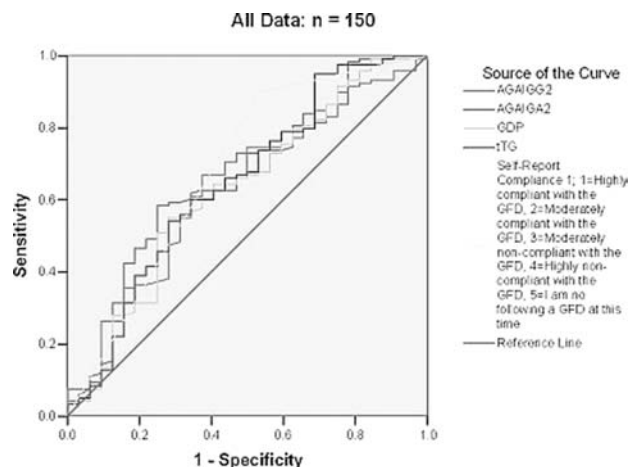
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**Purpose:** In recent years increasing number of individuals have been diagnosed with celiac disease (CD). The only accepted treatment for CD is lifelong adherence to a strict gluten-free diet (GFD). Adherence to the GFD is known to be variable however data guiding the assessment of compliance is currently lacking. We sought to determine the predictive value of self-report and four serologic tests compared to expert nutritionist evaluation.

**Methods:** 154 individuals between the ages of 22 and 91 followed for biopsy proven celiac disease were enrolled in the study. All participants were asked to rate their adherence to a GFD on a likert scale. They then underwent a standardized evaluation by a nutritionist with expertise in celiac disease blinded to the participants self-rated adherence. Blood was then drawn and tested for titers of IgA tissue transglutaminase (tTG) antibody, IgA and IgG deaminated anti-gliadin antibody (dAGA) and conjugated IgA-IgG dAGA. ANOVA and ROC analyses were conducted to determine the value of the different measures in determining adherence level.

**Results:** All serologic measures as well as participant reported adherence were significantly associated with GFD adherence as measured by nutritionist evaluation with Spearman's correlation,  $P = < 0.001, 0.002, 0.010, 0.015, 0.017$  for self-report, IgA-dADA, IgA-IgG dAGA, IgA-tTG and IgG dAGA, respectively. On ROC analysis however, no measure performed satisfactorily. For a set sensitivity of 80%, a cutoff value of 17.0 for IgA dADA yielded a specificity of 58%, a cutoff value of 10.4 for IgG dADA yielded a specificity of 54%, a cutoff value of 15.0 for GDP yielded a specificity of 50%, and a cutoff value of 18.5 for IgA tTG yielded a specificity of 56%. (see Fig. 1) The performance of all serologic testing but not self-report improved with increased time on the GFD.

**Conclusion:** Although current serologic tests have very high sensitivities and specificities for the diagnosis of celiac disease, they cannot replace trained nutritionist evaluation in the assessment of GFD adherence.[figure 1]



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### Unusual Reasons for Incomplete Colonoscopy

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**Purpose:** A 50 year old woman had h/o chronic constipation for 15 years. She could not have any bowel movement without the use of laxatives. She has been using laxatives daily for 15 years but she assured us that she only used a "safe, natural, herbal" laxative. There was no h/o hematemesis, melena or hematochezia. There were no constitutional symptoms. There were no other GI complaints, there was no F/H of colon cancer. The review of systems was unremarkable. Physical Examination was normal. CBC & Chemistry panel was normal. A screening colonoscopy was performed after usual PEG preparation. The rectum and the sigmoid colon were very dark due to severe melanosis coli. As the scope entered the descending colon, the view became pitch dark; the endoscopist felt he was in a jungle at night without a flash light. Manually increasing the brightness to the maximum on the light source did not help. The procedure was abandoned. Biopsies were obtained in the sigmoid colon. Later on an elective BE ruled out any masses or polyps in the rest of the colon. The histologic examination of the biopsy showed extensive infiltration of the cells in the lamina propria & submucosa with pigment. On further questioning, the patient informed us that she has been using Nature's Secret—Super Cleanse laxative which she said had natural herbs. An evaluation of the composition of Super-Cleanse showed it contained Cascara sagrada bark which is rich in anthraquinones & anthracene which are known to cause melanosis coli.

**Methods:** This is an unusual case in that SEVERE melanosis coli prevented completion of screening colonoscopy. The exact composition of so called "natural, herbal, safe" laxatives should be ascertained: besides cascara sagrada other herbs such as Aloe vera and Senna (Swiss Kriss) may contain chemicals which can cause melanosis coli & other serious side effects. The pigment in melanosis coli is not melanin so it should be called pseudo-melanosis coli. Melanosis coli involving pericolic lymph nodes associated with the herbal laxative Swiss Kriss has been reported in a patient with colonic adenocarcinoma (Arch Path lab Med 128:565–567, 2004). Rarely melanosis may involve other parts of the GI tract such as the ileum, esophagus & stomach. It may also involve the Vagina & Prostate. Anthraquinone-induced apoptosis of colonic epithelial cells may be important in pathogenesis. (Am J Path, 131:465–476, 1988).

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### Treatment of Symptomatic Small Intestinal Bacterial Overgrowth and Weight Gain after Gastric Bypass Surgery

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**Purpose:** We reported that daily oral thiamine is not effective for treating thiamine deficiency after Roux-en-Y gastric bypass surgery (GPS); in contrast, in those patients with abnormal glucose-hydrogen breath tests, antibiotic therapy with oral thiamine is effective therapy. Small intestinal bacterial overgrowth (SIBO) interferes with micronutrient and macronutrient absorption from the small intestine and may reduce caloric intake. We hypothesize that antibiotic therapy for SIBO induces weight gain after GBS.

**Methods:** In this retrospective chart review; 17 female patients (age range 33–65 years; mean age 51 years) had Roux-en-Y GBS in 1999–2005. The study included: 1) post-operative patients who had both an abnormal glucose-hydrogen breath test and abdominal symptoms consistent with SIBO, who 2) received an antibiotic to treat bacterial overgrowth. Antibiotic was given for 7 to 10 days, once monthly. Sex, age, weight before and after receiving antibiotic, and the presence of or resolution of abdominal symptoms after antibiotic were recorded. Abnormal glucose-hydrogen breath test was defined by increase in breath hydrogen >20 ppm within 45 minutes after 50 grams glucose. Patients were seen 8 to 72 months after GBS (mean: 32 months). Resolution of abdominal symptoms was used to determine effectiveness of antibiotic therapy.

**Results:** Eight patients had weight gain (range: 0.5–7.2 kg; mean: 3.2 kg) 2 to 5 months (mean: 3.1 months) after beginning antibiotic therapy. Among these 8 patients, abdominal symptoms resolved in 7; among 9 patients with weight loss, only 3 had resolution of abdominal symptoms (Chi-squared  $2 \times 2$ :  $P = .03$ ). Nine patients had weight loss of 0.5 to 14.4 kg (mean: 4.6 kg) at 2 to 4 months (mean: 3.1 months). Abdominal symptoms resolved in 7 of 13 patients receiving metronidazole, 1 of 2 with amoxicillin/clavulanate, and 2 of 2 with rifaximin.

**Conclusion:** Weight gain in patients with SIBO receiving antibiotics was associated with resolution of abdominal symptoms. This supports our hypothesis that antibiotic treatment of bacterial overgrowth induces weight gain. Conversely, SIBO may promote weight loss after GBS. Weight gain noted after antibiotic treatment could be due to: increased caloric intake, resolution of abdominal symptoms, or increased macronutrient absorption.

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### Celiac Disease in the Adult Community; Still a Rare Occurrence

*Douglas J. Sprung, MD\*, Gregory M. Sprung, Maitland, FL.*

**Purpose:** To evaluate the prevalence of Celiac disease (CD) in a general community gastroenterology practice in Orlando, FL.

**Methods:** A retrospective computer review of all patient charts in our single specialty gastroenterology practice, with a diagnosis of CD was undertaken. Charts from 1/91 – 12/05 were reviewed. A diagnostic small bowel biopsy (SBB) or positive anti-gliadin Ab plus anti-endomysial Ab (or anti-tTg Ab) were required for the diagnosis of CD. All characteristics, symptoms and laboratory values were examined.

**Results:** Of 70 patients with a computer diagnosis of CD, 30 charts were unavailable because they had been shredded due to inactivity for 7 years or more, or left the practice with a former partner. Of the remaining 40 patients, 10 did not meet criteria. 30 charts were reviewed. 11 (36%) were male, 19 (64%) female. The mean age was 55. The diagnosis of CD was made by blood tests alone in 4 patients, by SBB alone in 11, and by both in 15. Diarrhea occurred in 23 (70%), weight loss in 16 (53%) and anemia in 20 (66%). Anemia was borderline in 10, moderate in 2, severe in 1, iron deficient in 6 and macrocytic in 1. One patient had concomitant Crohn's disease (and dermatitis herpetiformis) and 4 had concomitant microscopic colitis. None developed cancer, requires steroids or failed to improve on a gluten free diet. Each physician diagnosed 1.3 patients with CD per year. A review of all SBB done over a one year period at a single community hospital revealed 3 cases of CD out of 570 patients, or a prevalence of 1/190. These were symptomatic patients who underwent gastroscopy.

**Conclusion:** 1. In a private adult GI practice, CD was a relatively rare diagnosis over a 15 year period. The average number of cases per year has remained stable. 2. The triad of diarrhea, weight loss and anemia was present in over 60% of patients, with 97% of all patients having at least one of these findings. 3. Microscopic colitis was the most common concomitant illness, Crohn's disease occurred concomitantly in only one instance. 4. Out of 570 symptomatic patients who underwent SBB to rule out CD, only 3 were positive (0.5%). 5. CD remains an uncommon diagnosis in the private community sector, with no evidence of an increasing prevalence over the past 15 years. It seems unlikely that there are a significant number of patients who go undiagnosed as has been suggested in the literature.

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### Mechanism of Zinc Deficiency in Patients with Roux-en-Y Gastric Bypass Surgery

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**Purpose:** Zinc is an essential component of the catalytic site of hundreds of different metalloenzymes where it functions as a Lewis acid. The small intestine is the main site of zinc absorption via transporter expression which is regulated by dietary zinc intake.

It has been reported that some patients become zinc deficient after Roux-en-Y gastric bypass, although the mechanism of this is unknown. Based on our ongoing work examining thiamine deficiency, we hypothesize that small bowel bacterial overgrowth can decrease small intestinal zinc absorption.

**Methods:** This is a retrospective review of 452 patients who underwent Roux-en-Y gastric bypass surgery from 1999–2005. All patients were identified who had measurement of serum folate levels. As a marker of small intestinal bacterial overgrowth (SIBO), elevated serum folate level (>14 ng/dL) has a reported specificity of 79%. Baseline patient demographics and characteristics including age, sex, BMI were recorded. There were 230 patients who had determination of serum folate level, and 172 patients who had both serum folate and serum zinc levels.

**Results:** There were 199 female and 31 male patients with average age of 46 years (range: 21–68 years). The mean body mass index was 53 kg/m<sup>2</sup> (range: 40–100). Of these 230 patients, 145 had elevated serum folate levels supporting a prevalence of 63% for SIBO. Of the 172 patients who also had serum zinc levels, in 54 patients with normal serum folate levels, 43 had normal serum zinc; among 118 patients with elevated serum folate, 78 had low serum zinc (Chi-squared  $2 \times 2$ :  $P < .001$ ).

**Conclusion:** Elevated serum folate, a marker for small intestinal bacterial overgrowth, is common after gastric bypass surgery. This study supports our hypothesis that small bowel bacterial overgrowth can decrease small intestinal zinc absorption. Since present physiological evidence supports zinc absorption primarily in the jejunum by a transcellular route involving a zinc-specific transporter, Zip4, further studies should be directed at potential post-operative changes in zinc transport and the potential for reversibility with treatment of small intestinal bacterial overgrowth.

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### The Efficacy of the GLP-1 Agonist Exenatide in the Treatment of Short Bowel Syndrome

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**Purpose:** Short bowel syndrome (SBS) is a serious medical problem resulting in severe diarrhea and nutritional deprivation. The symptoms result from

lack of absorptive surface and loss of the braking mechanisms controlling the proximal gut. One of the missing, distally produced, peptides that control the proximal gut is glucagon-like peptide-1 (GLP-1). In this study we test the effect of the GLP-1 receptor agonist, exenatide, on short bowel syndrome.

**Methods:** SBS subjects were selected based on clinical symptoms and greater than 50% distal small bowel resection. Before beginning exenatide treatment, each patient completed a questionnaire documenting stool frequency and consistency. In addition, SBS symptoms, CBC, chemistries and BMI were also obtained. An antroduodenal manometry study was performed during fasting, after exenatide, and after a subsequent test meal. Each patient was then started on exenatide 5 to 10 mcg subcutaneously twice a day. Over the following month the baseline parameters measured were repeated.

**Results:** The subjects consisted of 4 males and 1 female, ages 46 to 69 (mean: 57.2). At baseline, all patients had severe diarrhea that ranged from 7 to 15 bowel movements per day, often occurring within 15 minutes of eating. After exenatide, all 5 patients had an immediate improvement in bowel frequency and form. In the most severely affected patient, the bowel movements reduced from 15 watery bowel movements per day to 2–3 formed stool. In all subjects, bowel movements were no longer meal related and often occurred hours after any meal. At baseline nutritional parameters were stable due to total parenteral nutrition (TPN) in most cases (N = 3). However, after exenatide, all 3 patients no longer needed TPN. Despite the lack of TPN, no weight loss or biochemical nutritional deterioration was observed in any case. Previous attempts at ceasing TPN had resulted in immediate and life-threatening dehydration and malnutrition. Using normal bowel function as a goal, subjects described their improvement with exenatide as 65–100% improved. Antroduodenal manometry in 2 out of 5 subjects demonstrated continuous low amplitude gastric contractions during fasting which completely normalized after exenatide.

**Conclusion:** Exenatide is a novel and safe treatment option for SBS. It normalizes bowel function and maintains nutritional status. Successful treatment with exenatide may significantly reduce the need for parenteral nutrition.

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### Calcium Deficiency Is Associated with Small Intestinal Bacterial Overgrowth after Roux-en-Y Gastric Bypass Surgery

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**Purpose:** We have shown that after Roux-en-Y gastric bypass surgery (GBS), patients frequently have elevated serum folate levels, a marker of small intestinal bacterial overgrowth (SIBO). Gastric pouch achlorhydria after GBS may lead to SIBO. Calcium deficiency with subsequent hyperparathyroidism and decreased bone mineral density has been reported after GBS. We hypothesize that by altering gut ecology, GBS induces calcium deficiency.

**Methods:** This is a retrospective chart review of 452 patients who underwent Roux-en-Y gastric bypass surgery from 1999–2005. Of these patients, 154 had determination of serum folate, serum calcium, and 24 hour urinary calcium levels. Baseline patient demographics and characteristics included age, sex, and BMI. Glucose-hydrogen breath testing (HBT) had been performed in 43 patients (abnormal test was: hydrogen concentration >15 ppm over baseline fasting value or fasting hydrogen level >10 ppm).

**Results:** In 129 female and 25 male patients, average age was 42 years (21 to 63 years) with BMI range of 40 to 80 kg/m<sup>2</sup>. Among 43 patients who underwent HBT, 42 had an abnormal breath test. Of these 42 patients, 38 also had elevated serum folate (90% sensitivity for elevated serum folate as a predictor of SIBO). Of 42 patients with abnormal HBT, 30 had low 24 hour urinary calcium (Chi-squared 2 × 2: *P* < .01). In the 154 patients, 48 patients had normal serum folate levels of whom 38 had normal urinary calcium; in 106 patients with elevated serum folate, 80 had low 24 hour urinary calcium

(Chi-squared 2 × 2: *P* < .001). Corrected serum calcium was within the normal range in all patients.

**Conclusion:** Using HBT as the gold standard, almost all GBS patients who were tested had abnormal HBT, supporting the belief that SIBO is common after GBS. Elevated serum folate has a high sensitivity for detecting SIBO. Serum calcium determination is not accurate in predicting calcium metabolism in these patients. This study supports our hypothesis that by altering gut ecology, GBS induces calcium deficiency. Calcium malabsorption and secondary hyperparathyroidism may increase the risk for developing osteopenia, osteoporosis, and ultimately osteomalacia. Further studies of calcium metabolism after treatment of SIBO may support a treatment option for these patients.

## 235

### A Systematic Review of Diagnostic Testing for Small Intestinal Bacterial Overgrowth

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**Purpose:** There is a growing body of literature investigating the role of small intestinal bacterial overgrowth (SIBO) in various disease states. However, there is much criticism regarding the diagnostic accuracy of testing. The aim of this study was to systematically review the validity of diagnostic tests for SIBO.

**Methods:** We performed an electronic literature search of U.S. National library of medicine (PubMed) and OVID Medline using key words to identify and capture a broad series of article titles related to the diagnosis of bacterial overgrowth. An *a priori* set of inclusion and exclusion criteria were applied to titles, abstracts and subsequently papers to determine those for final review. The papers included in the final selection were categorized by type of diagnostic test and evaluated for consistency and design. In the final step of the review, the studies were compared to published guidelines for expectations of publications evaluating a diagnostic test (Reid, et al).

**Results:** With the initial electronic search, 1485 abstract titles met preset key words. After stepwise application of criteria for abstracts and papers, 71 met the standard for inclusion. Many studies had less than 20 subjects and often a mixture of diseases predisposing to SIBO. There was no study that properly validated culture at 10<sup>5</sup> cfu/mL in upper bowel for SIBO. There was great variability on culturing techniques and aspirate location. One reasonably sized study demonstrated that controls had no bacteria, celiac had 10<sup>1</sup>, IBS 10<sup>3</sup> and only Billroth II patients demonstrated levels greater than 10<sup>5</sup> (Bardhan, et al). Given the lack of gold standard, it was difficult to validate all other testing such as breath test. Another technique for evaluating the accuracy of diagnostic testing was to retest after treatment with antibiotic. 23 of the 71 papers studied the test utility in this way and were most convincing of the clinical utility for the specific test used. Finally, using published standards for an accurate diagnostic test, none of the 71 publications fulfilled the full set of criteria.

**Conclusion:** Diagnosis of bacterial overgrowth has no gold standard since even culture has not been properly evaluated. In the absence of a gold standard, this study suggests that clinical correlation in a test, treat and retest situation is the best method for the management of bacterial overgrowth until more accurate diagnostic testing is available.

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### Genetic Testing Prior to Serologic Screening in Family Members of Patients with Celiac Disease as a Cost Containment Method

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**Purpose:** Family members of patients with celiac disease (CD) have increased rates of developing CD over their lifetime, with up to 3%

seroconverting 5 years after an initial negative result. Repeat testing of family members 5 years later would improve CD diagnosis rates, but at significant cost. Genetic testing prior to screening family members for CD would potentially reduce these screening costs by eliminating HLA-DQ2 and DQ8 negative patients who are at extremely low risk for developing CD.

**Methods:** Decision analysis was used to compare the costs of screening family members of patients with CD. The decision tree incorporated three diagnostic branches: initial screening with anti-tissue transglutaminase (tTG), repeat screening with tTG at 5 years later, and genetic testing prior to screening with tTG. Costs were estimated using Medicare reimbursement fees. Modeling and sensitivity analyses were performed using Tree Age Pro 2006 (Williamstown, MA).

**Results:** The cost of an initial screening with tTG of family members of patients with CD is approximately \$434 per person. Repeat screening at 5 years later would cost \$683 per person, which is an additional \$249, but would diagnosis an additional 4.4% cases of CD. Genetic testing prior to screening family members would be slightly more costly, at \$750 per person, but would lower endoscopy workload by nearly 25% when compared to repeat screening at 5 years without genetic testing. The cost of genetic testing would have to decrease from \$301.40 to \$234.40, a difference of \$67, to justify its use prior to serologic testing. As the specificity of tTG approaches 100%, the cost of genetic testing would have to continue to decrease to less than \$200 in order for it to be an affordable option.

**Conclusion:** Repeat screening with tTG of family members of patients with CD results in a significant increase in cost, but also an associated increase in CD cases diagnosed. Genetic testing would potentially eliminate up to 60% of the population to be screened and, if available at a lower cost, would partially offset costs of repeat serologic screening.

sis (81.8%) and increased lamina propria infiltrate in the duodenal mucosa. Electron microscopy showed distorted microvilli, dilated mitochondria, increased rough endoplasmic reticulum in alcoholic pancreatitis patients.

**Conclusion:** Chronic alcoholic pancreatitis patients showed significant alteration in duodenal mucosal enzyme activities indicating injury to enterocytes. These observations were supported by the light microscopic and ultrastructural alteration of enterocytes.

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#### Pathomorphologic and Functional Alteration of Duodenal Mucosa in Patients with Chronic Alcoholic Pancreatitis

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**Purpose:** Since the pathomorphologic and functional alteration of duodenal mucosa among chronic alcoholic pancreatitis patients is unknown, therefore we studied duodenal mucosal morphologic alteration and enzyme activities of chronic alcoholic pancreatitis patients.

**Methods:** This prospective study included diagnosed cases of chronic alcoholic pancreatitis (N = 11) in whom duodenal biopsies were studied for brush border enzymes (disaccharidases, alkaline phosphatase, LAP, LDH, GGT), intracellular enzymes (G-6-PDH, ICDH, G-6-P), membranous enzyme (Na<sup>+</sup>-K<sup>+</sup> ATPase) activities and pathomorphologic (light microscopic and ultrastructural) alterations. The duodenal biopsy from patients with GERD (N = 29) were taken as control. The results were expressed as number and percentage or mean  $\pm$  SEM. Appropriate statistical methods were applied. Informed written consent was obtained prior to participation in study. The study was approved by the Institute ethical committee.

**Results:** The mean age (all males) of patients was  $41.0 \pm 10.7$  years. The mean duration of alcohol intake was 250 ml/day for  $14 \pm 1.3$  years. In duodenal mucosa of pancreatitis and GERD patients the mean enzymatic activities (IU/g protein) of lactase was  $6.2 \pm 0.5$  Vs  $24.3 \pm 1.0$  ( $P < 0.001$ ), sucrase was  $18.6 \pm 1.7$  Vs  $42.4 \pm 1.8$  ( $P < 0.001$ ), maltase was  $35.4 \pm 2.2$  Vs  $76.1 \pm 13.0$  ( $P < 0.001$ ), LAP was  $140.0 \pm 9.8$  Vs  $27.7 \pm 17.6$  ( $P < 0.01$ ), LDH was  $402.0 \pm 40.2$  Vs  $104.9 \pm 4.1$  ( $P < 0.001$ ), GGT was  $208.1 \pm 11.2$  Vs  $99.5 \pm 4.2$  ( $P < 0.001$ ) and alkaline phosphatase was  $267.4 \pm 11.3$  Vs  $180.6 \pm 6.5$  KAU/g protein ( $P < 0.01$ ). The mean enzymatic activities in duodenal mucosa of pancreatitis and GERD patients for G-6-PDH was  $4.4 \pm 0.4$  Vs  $11.0 \pm 0.2$  ( $P < 0.001$ ), ICDH was  $13.8 \pm 0.5$  Vs  $23.2 \pm 1.6$  ( $P < 0.05$ ), G-6-P was  $0.6 \pm 0.06$  Vs  $1.7 \pm 0.05$  ( $P < 0.001$ ) and Na<sup>+</sup>-K<sup>+</sup> ATPase was  $1.1 \pm 0.01$  Vs  $2.5 \pm 0.09$  ( $P < 0.001$ ). Chronic alcoholic pancreatitis patients showed mild villous atrophy (36.4%), intraepithelial lymphocyto-

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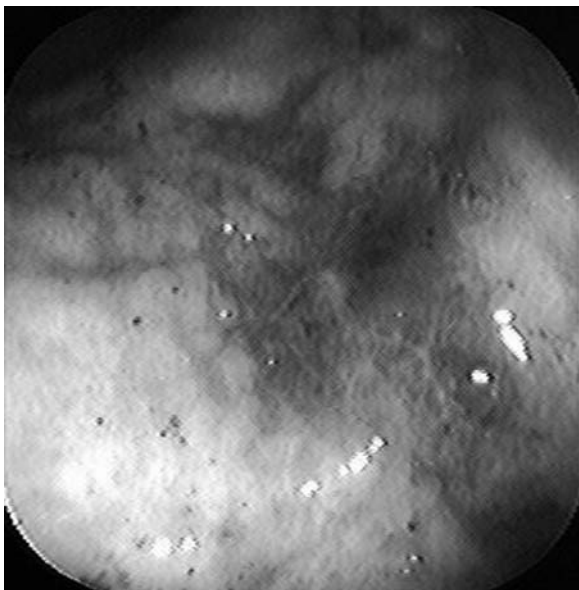
ABSTRACT WITHDRAWN

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**Massive Upper GI Bleed and Duodenal Ulcer Caused by Intra-Hepatic Artery Infusion Catheter Eroding into Duodenum in a Patient with Metastatic Colorectal Cancer**

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**Purpose:** Intra-hepatic arterial infusion (HAI) pump placement for selective hepatic chemotherapy in patients with metastatic colorectal cancer has been previously used and was associated with many complications. We report for the first time a case where a HAI catheter eroded into the duodenum causing ulceration and massive upper GI bleeding.

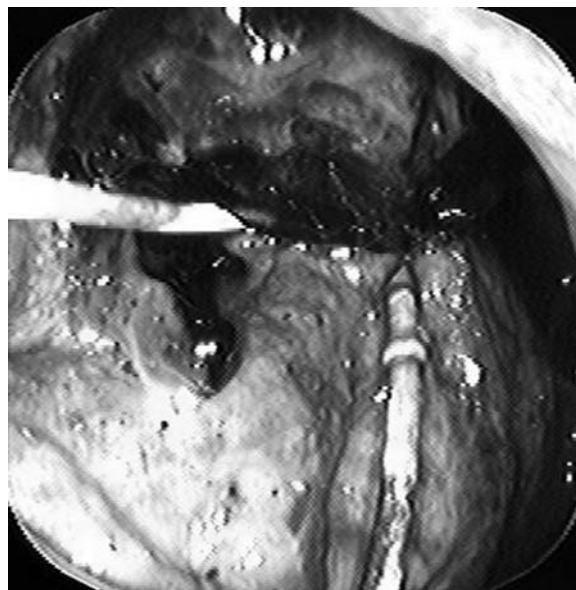


**Methods:** A 61-year-old Hispanic female presented for evaluation of mild abdominal pain and vomiting for three days. Her past medical history was significant for colon cancer with metastases to the liver. She was treated with multiple colonic resections, subtotal hepatic resection and eventual placement of a HAI pump 5 years ago. The patient had repeated episodes of

bowel obstruction over the past several years in addition to multiple series of sepsis and peritonitis. It was determined upon admission to perform lysis of adhesions and side-to-side enteroenterostomy. Several days later, the post-surgical fistula presented with an upper GI bleed with hemostatic instability and requiring multiple transfusions.

**Results:** At endoscopy, multiple clean based antral and body gastric ulcers were noted in addition to diffuse hemorrhagic gastritis (Fig. 1). The previously placed intra-hepatic artery infusion catheter was seen protruding into the bulb of the duodenum surrounded by a large clot and ulceration (Fig. 2).

**Conclusion:** In our finding of duodenal ulceration and upper GI bleed, the catheter was found lodged adjacent to blood clot in a coiled shape. We believed that this was a result of direct trauma by the eroding catheter into the duodenum. It was first time this kind of complication from Intra-hepatic arterial infusion catheter has been reported in USA.[figure1][figure2]



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**A Case of Large Hookworm Infestation**

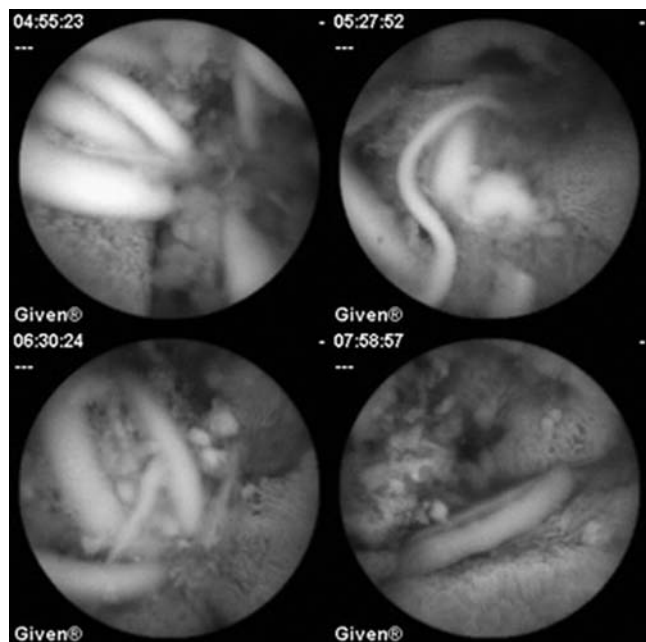
Gourisankar P. Degala, MD, Osama Alaradi, MD\*. *Gastroenterology, Henry Ford Health System, Detroit, MI.*

**Purpose:** A forty-four year old Caucasian female patient presented with few year history of recurrent abdominal pain and bouts of intestinal obstruction for which she underwent multiple abdominal surgeries. She was noted to have microcytic anemia on laboratory studies: Hemoglobin 9.9 g/dL, MCV 78.1 fl, Iron 14 ug/dL and ferritin of 7 ng/ml (Normal 10–120 ng/mL). Her endoscopic evaluation for GI blood loss included EGD and Colonoscopy. Both were normal. A small bowel follow-through evaluation showed post-surgical changes. Subsequently, a small bowel capsule endoscopy (Given Imaging, Yoqneam, Israel) was performed without any complication. An interpretation of the images revealed the results seen in Figure A.

Multiple adult worms were seen in the small intestine. Worms, worm fragments, and hooklets were seen in the distal small intestine. There were multiple erythematous areas where the worms were seen. The worms were present in the study for three hours and thirty minutes. The capsule did not make it into the colon by the end of the study but a subsequent abdominal film showed that it passed.

Two separate stool studies for ova and parasites were negative for helminthic eggs. The patient also denied ever passing worms in her stool. The patient had no significant travel history but did have worm infestation when she was seven years old. A microbiologist examined the pictures and confirmed that

the morphology of the organisms was consistent with hookworms, likely *Necator americanus*. She was treated with two courses of albendazole. This case is a demonstration of a significant abnormal finding in the small intestine diagnosed only with capsule endoscopy. The high worm load was clearly the source of iron deficiency anemia. The delayed capsule transit time also raises questions of whether the worm load delayed motility or caused a low-grade intestinal obstruction. This is the largest worm load we have seen compared to previously described cases.[figure1]



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### Risk Factors for Small Intestinal Bacterial Overgrowth

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**Purpose:** Small intestinal bacterial overgrowth (SIBO) has been associated with various gastrointestinal disorders. Enteric bacterial flora are thought to play an important role in the pathogenesis of some gastrointestinal diseases. We aim to determine which patient characteristics, symptoms, and laboratory values are predictive of SIBO as defined by a positive glucose breath test.

**Methods:** The records of all patients who were referred for a glucose breath test between January 1, 2003, and December 31, 2006, were analyzed retrospectively. Breath samples were analyzed for hydrogen and methane using a Model DP Microlyzer (Quintron Instrument, Milwaukee, WI). A breath test was deemed positive when the baseline hydrogen or methane value increased by greater than 12 ppm after the ingestion of 50 g of glucose. Chi-square tests and Fisher's exact test were used to determine associations between categorical variables. The independent sample t-test was used to compare groups of continuous variables.

**Results:** Of the 167 eligible patients who were referred for a glucose breath test, 139 patient records were available for analysis (49 male, 90 female; mean age  $54 \pm 13$  years). There were 40 patients (29%) with positive breath tests. Patient characteristics that were significantly associated with a positive glucose breath test were: age greater than 75 years ( $P = 0.01$ ), low serum albumin ( $P = 0.04$ ), and a history of cirrhosis ( $P = 0.02$ ). The OR for age greater than 75 was 4.7 (95% CI 1.4, 15.4). A history of irritable bowel syndrome significantly lowered the risk of a positive test (OR = 0.27,  $P = 0.02$ ). There was no association between a positive breath test and the use of proton pump inhibitors, histamine-2 receptor antagonists or antimotility

drugs. Diarrhea was significantly associated with a positive breath test by hydrogen criteria (OR 2.9,  $P = 0.01$ ), but no similar association was found with constipation, abdominal pain, bloating or gas.

**Conclusion:** In this patient cohort, advanced age, low albumin and a history of cirrhosis were significantly associated with a positive glucose breath test. Patients with IBS were less likely to have a positive breath test. Knowledge of the predisposing factors for SIBO might lead to earlier testing and treatment in some patients.

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### Can Colorectal Cancer Screening Consultations Assist in Evaluating Physician Adherence to Management of Obese African American Patients?

Anita Mittal, MD, Rebecca Fausel, Marie L. Borum, MD, MPH, EdH\*. Internal Medicine, University of Hawaii, Honolulu, HI and Gastroenterology, The George Washington University School of Medicine, Washington, DC.

**Purpose:** Obesity is an epidemic in the United States that causes significant morbidity and mortality. It is estimated to cost the nation billions annually. Two thirds of American adults are considered overweight/obese. It has been suggested that certain ethnic groups, especially African Americans, are less likely to receive weight management. This study evaluated the prevalence of overweight/obese African American patients seeking colorectal cancer screening and the frequency of physician recommended weight management.

**Methods:** A retrospective medical chart review was performed where medical records of consecutive patients referred to a continuity GI clinic for colorectal cancer screening during a three-month period were evaluated. Documentation regarding demographics and weight management was put into a database, with patient anonymity maintained. Statistical analysis was performed with significance determined at  $P < 0.05$ .

**Results:** Our results showed a significant difference in the prevalence of obesity between African American males and females ( $P < 0.05$ ), and a significant difference in the frequency of physician directed weight management, with males not receiving as much counseling ( $P < 0.01$ ).

**Conclusion:** Literature reveals that African Americans are less likely to receive preventative health care. Colorectal cancer screening can be used to find and aid these populations not being counseled, therefore improving health care and potentially reducing the complications and cost caused by obesity.

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### Absorption and Metabolism of Acetate, Glucose, and Amino Acid in Metabolic Syndrome

Yoshihisa Urita, Toshiyasu Watanabe, Tadashi Maeda, Kaoru Doman, Susumu Ishihara, Tomohiro Arita, Asuka Nakayama, Makie Nanami, Tatsuhiko Yamamoto, Akiro Kugahara, Takamasa Ishii, Hirohito Kato, Kazuo Hike, Noriko Hara, Yoshiko Honda, Kazushige Nakanishi, Nagato Shimada, Motonobu Sugimoto\*, Kazumasa Miki. Department of General Medicine and Emergency Care, Toho University, Tokyo, Japan; Division of Gastroenterology and Hepatology, Department of Internal Medicine, Toho University, Tokyo, Japan and Department of Hematology, Toho University, Tokyo, Japan.

**Purpose:** The aim of this study is to evaluate the absorption and metabolism of nutrients in patients suspicious of metabolic syndrome.

**Methods:** Consecutive 230 subjects presenting diagnostic upper endoscopy were recruited in this study.  $^{13}\text{C}$ -acetate was administered intraduodenally in 78,  $^{13}\text{C}$ -glycine in 65, and  $^{13}\text{C}$ -glucose in 77 patients. At the end of endoscopy, a tip of endoscope was placed to the second part of the duodenum and 20 ml of water containing 100 mg of  $^{13}\text{C}$ -substrate was sprayed onto the duodenal mucosa. Breath samples were taken at baseline and at 10-min interval. Next,  $^{13}\text{C}$ -acetate breath test, in which the substrate was orally

administrated with 100 cc of water, was performed in patients with fatty liver diseases and viral hepatitis.

**Results:** A delay in the  $^{13}\text{C}$ CO<sub>2</sub> excretion curve in patients with BMI of more than 26 was found after administration of  $^{13}\text{C}$ -acetate, whereas an increased  $^{13}\text{C}$ CO<sub>2</sub> excretion was noted in obese patients after administration of  $^{13}\text{C}$ -glycine. For  $^{13}\text{C}$ -acetate breath test, there was a significant delay in  $^{13}\text{C}$ CO<sub>2</sub> excretion in patients with fatty liver as compared with viral hepatitis and healthy volunteers.

**Conclusion:** These results suggest that  $^{13}\text{C}$ -acetate breath test may be useful for the screening of metabolic syndrome.

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### Can Colorectal Cancer Screening Assist in Evaluating Physician Adherence to Guidelines for Ordering DEXA Scans?

Anita Mittal, MD, Rebecca Fausel, Marie L. Borum, MD, MPH, EdH\*.

Internal Medicine, University of Hawaii, Honolulu, HI and Gastroenterology, The George Washington University School of Medicine, Washington, DC.

**Purpose:** There are significant health disparities between African Americans and whites, in the United States. Colon cancer screening can aid in decreasing the morbidity and mortality from colon cancer, and may also identify other health risks during gastroenterology consultations. This study evaluated the prevalence of African American and Caucasian women who require a DEXA scan seeking preventative care colorectal cancer screening and the frequency of physician ordered DEXA.

**Methods:** After IRB approval, medical records of consecutive female patients referred to a continuity GI clinic for colon cancer screening consultations during a three-month period were evaluated for documentation on whether a DEXA was ordered, not ordered, or not needed. A Microsoft Excel database was created, with patient anonymity maintained. Statistical analysis was performed using chi-square with a significance set at  $P < 0.05$ .

**Results:** 35.5% of Caucasian women did not receive a DEXA who needed it, whereas 39.3% of African American did not get a DEXA. The results showed a trend towards African American women being less likely to receive a screening DEXA when they needed it, with  $P$ -value  $< 1$ .

**Conclusion:** Although there was not a significant difference between the number of African American and Caucasian women who received a DEXA, our study revealed that over a third of these women should have received one regardless of ethnicity, but did not. Colorectal cancer screening can be used as a tool to detect these women and make sure that they get optimal care.

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### Nitazoxanide for the Treatment of SIBO Related Gastrointestinal Symptoms in Pediatric Population

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**Purpose:** Many pediatric patients present with symptoms of Small Intestinal Bacterial Overgrowth (SIBO). Intestinal anaerobic bacteria are known to contribute to the symptoms exhibited by these patients. However, without a definitive test to confirm SIBO, many pediatric practitioners empirically treat these patients with a course of antibiotics with or without probiotics. Nitazoxanide (NTZ) is a first in class thiazolide antibiotic with a targeted anaerobic antibacterial activity, placebo-like safety profile, high gastrointestinal (GI) concentration, and has limited to no activity against probiotic species. To date no studies have evaluated the empiric use of NTZ for the treatment of GI related symptoms in pediatric SIBO patients.

**Methods:** A chart review was performed on patients treated with NTZ from February 2006 to May 2007. The diagnosis of SIBO was made by the attend-

ing physician based on the patient's history, signs and symptoms. Efficacy was measured as resolution of the patient's GI related symptoms, 3–8 weeks after the end of therapy. Primary markers for resolution included: abdominal pain, diarrhea, constipation, bloating, and/or flatulence. Overall 22 patients met the inclusion criteria for review.

**Results:** Of the 22 patients treated with NTZ, 13 (median age – 6.8 years) patients returned to the office for adequate follow up. Nine patients were prescribed NTZ for SIBO and have not returned to the office for any GI complaints. The range of NTZ doses used was 100 mg – 500 mg BID for 5–10 days depending on age of the pediatric patient. The mean dose and duration was 422 mg/d for 7.7 days. The most common dose was 200 mg BID for 10 Days ( $N = 5$ ). All patients treated with NTZ and a probiotic (13/13 [100%]) had complete resolution of symptoms that were present at initial visit.

No clinically significant adverse reactions attributable to NTZ were identified during the study.

**Conclusion:** Nitazoxanide appears to be a safe and effective therapy for the empiric treatment of SIBO related GI symptoms in pediatric patients. Larger controlled clinical trials are warranted to support these findings.

Symptoms	Results	
	Resolved or Improved	No Change / Worsen
Abdominal Pain	13/13 (100%)	N/A
Bloating	6/6 (100%)	N/A
Diarrhea	9/9 (100%)	N/A
Constipation	4/4 (100%)	N/A
Flatulence	5/5 (100%)	N/A

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### Effects of Liquid Meal Ingested Soon after Alcohol Ingestion on Alcohol Metabolism

Yoshihisa Urita, Toshiyasu Watanabe, Tadashi Maeda, Kaoru Domon, Susumu Ishihara, Tomohiro Arita, Asuka Nakayama, Makie Nanami, Tatsuhiro Yamamoto, Akiro Kugahara, Takamasa Ishii, Hirohito Kato, Kazuo Hike, Noriko Hara, Yoshiko Honda, Kazushige Nakanishi, Nagato Shimada, Motonobu Sugimoto\*, Kazumasa Miki. Department of General Medicine and Emergency Care, Toho University, Tokyo, Japan; Division of Gastroenterology and Hepatology, Department of Internal Medicine, Toho University, Tokyo, Japan and Department of Hematology, Toho University, Tokyo, Japan.

**Purpose:** Alcohol is commonly consumed with, or soon after, a meal that affects gastric emptying and thus, absorption and metabolism of alcohol. The aim of this study is to evaluate the effect of liquid test meal ingested soon after alcohol ingestion on alcohol metabolism, as is common in the social setting.

**Methods:** First, a 100 ml of water containing of 100 mg of  $^{13}\text{C}$ -ethanol was administrated orally in 5 healthy subjects and 2 diabetic patients, and 200 ml of liquid meal (Ensure Liquid) was administrated 5 min after  $^{13}\text{C}$ -ethanol ingestion. Breath samples were taken at baseline and at 10-min interval for 150 min. Next,  $^{13}\text{C}$ -ethanol breath test was performed without ingestion of liquid meal. Breath  $^{13}\text{C}$ CO<sub>2</sub> value was measured and expressed as delta over baseline (per mil).

**Results:** The peak value of  $^{13}\text{C}$ CO<sub>2</sub> excretion (Cmax) was decreased after ingestion of liquid meal in 5 of 7 patients, whereas the time of Cmax (Tmax) was unchanged. Only one patients had accelerated  $^{13}\text{C}$ CO<sub>2</sub> excretion after ingestion of liquid test meal. The descending gradient of  $^{13}\text{C}$ CO<sub>2</sub> excretion curves after ingestion of liquid meal is parallel to that without liquid meal.

**Conclusion:** These results indicated that liquid meal ingested soon after alcohol ingestion may not affect elimination but absorption and/or metabolism of a small amount of alcohol.

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### Relationship between Atrophic Gastritis and Fasting Breath Hydrogen and Methane Levels in the Elderly

Yoshihisa Urita, Toshiyasu Watanabe, Tadashi Maeda, Kaoru Domon, Susumu Ishihara, Tomohiro Arita, Asuka Nakayama, Makie Nanami, Tatsuhiro Yamamoto, Akiro Kugahara, Takamasa Ishii, Hirohito Kato, Kazuo Hike, Noriko Hara, Yoshiko Honda, Shuji Watanabe, Kazushige Nakanishi, Nagato Shimada, Motonobu Sugimoto\*, Kazumasa Miki.

Department of General Medicine and Emergency Care, Toho University, Tokyo, Japan; Division of Gastroenterology and Hepatology, Toho University, Tokyo, Japan and Department of Hematology, Toho University, Tokyo, Japan.

**Purpose:** Many factors contribute to inadequate nutrition, including health status, financial capacities, mobility, and physiologic needs. One of the most remarkable changes with aging is the frequent development of atrophic gastritis. This process was recently recognized to be due to *H. pylori* infection. The aim of this study was to investigate the relationship between atrophic gastritis and colonic bacterial alteration in the elderly.

**Methods:** Fasting breath hydrogen and methane levels and serum pepsinogens were measured in 560 *H. pylori*-seropositive patients. Serum pepsinogens (PG) were also measured to evaluate the grade of atrophic gastritis and gastric acid secretion.

**Results:** The fasting breath hydrogen level was  $4.0 \pm 7.0$  ppm highest in patients with a serum PG1/2 ratio of 3.5 to 4.0 and  $2.5 \pm 3.8$  ppm in those with a serum PG1/2 ratio less than 1.0. Similarly, there was no significant association between the serum PG1/2 ratio and fasting breath methane levels. When a patient had more than 10 ppm of  $H_2$  or  $CH_4$  levels, the patient was considered to have fermentation. The incidences of high intragastric  $H_2$  and/or  $CH_4$  levels were highest in patients with a serum PG1/2 ratio of 1.0 to 1.5. Among patients with a serum PG ratio less than 2.0, the increased fermentation was found in the younger group, whereas elder patients had more frequently increased fermentation among those with a serum PG1/2 ratio of 2.0 to 3.5 than younger groups.

**Conclusion:** In conclusion, although there was a close association between atrophic gastritis and bacterial overgrowth in the digestive tract in younger patients with *H. pylori* infection, factors other than the lack of gastric acid may have affect colonic fermentation in *H. pylori*-positive older patients.

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### Nitazoxanide for the Treatment of IBS and SIBO Related Gastrointestinal Symptoms

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**Purpose:** The definitive role of intestinal bacteria in Irritable Bowel Syndrome (IBS) has not been elucidated however clinicians routinely treat symptomatic IBS with antibiotics. Furthermore, Small Intestinal Bacterial Overgrowth (SIBO) contributes to the symptoms exhibited by many IBS patients. Without a definitive test to differentiate the two, many practitioners empirically treat these patients with a course of antibiotics and at times probiotics. Nitazoxanide (NTZ) is a first in class thiazolide antibiotic with a targeted anaerobic antibacterial activity, placebo-like safety profile, high gastrointestinal (GI) concentration, and limited to no activity against probiotic species. To date studies evaluating the empiric use of NTZ for the treatment of GI related symptoms in IBS and SIBO patients have not been presented.

**Methods:** A chart review was performed on patients treated with NTZ and assigned the following ICD-9 codes: 536.8, 564, 564.1, 787.3, 787.91, 789.07 between April 2006 and April 2007. The diagnosis of IBS and SIBO was made by the attending physician based on the patient's history, signs and symptoms. Efficacy was measured as improvement or resolution of the patient's GI related symptoms, 3–8 weeks after the end of therapy. Primary

markers for resolution included: abdominal pain, abdominal distension, diarrhea or constipation, and gas or bloating. A telephone questionnaire was used to determine resolution of symptoms in patients not followed up in person. Overall, 14 patients met the inclusion criteria for review.

**Results:** Of the 14 patients treated with NTZ, 12 were available for follow-up evaluation. The range of NTZ doses used was 500 mg BID-TID for 5–10 days. The mean dose and duration was 1097 mg/day for 8.2 days, the most common dose was 500 mg BID for 10 days (N = 6). Resolution of symptoms are outlined in Table 1. No clinically significant adverse reactions attributable to NTZ were identified during the study.

**Conclusion:** Nitazoxanide appears to be a safe and effective therapy for the empiric treatment of IBS and SIBO related GI symptoms. Larger controlled clinical trials are warranted to support these findings.

Table 1. Resolution of GI Symptoms

Symptoms	Resolved or Improved	No Change
Abdominal Pain	73% (8/11)	27% (3/11)
Abdominal Distension	67% (6/9)	33% (3/9)
Gas/ Bloating	83% (10/12)	17% (2/12)
Diarrhea/ Constipation	60% (6/10)	40% (4/10)

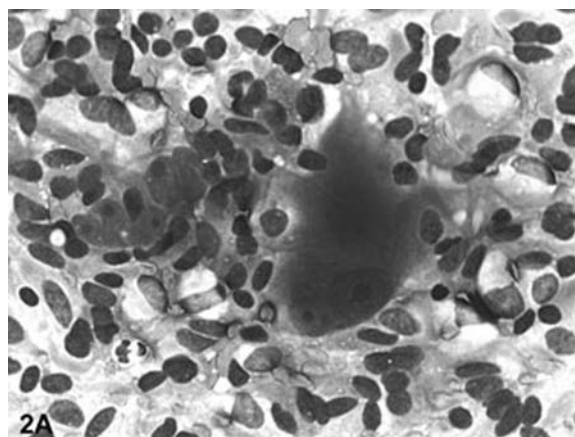
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### Fine-Needle Aspiration Biopsy of Duodenal Gangliocytic Paraganglioma: Report of Two Cases

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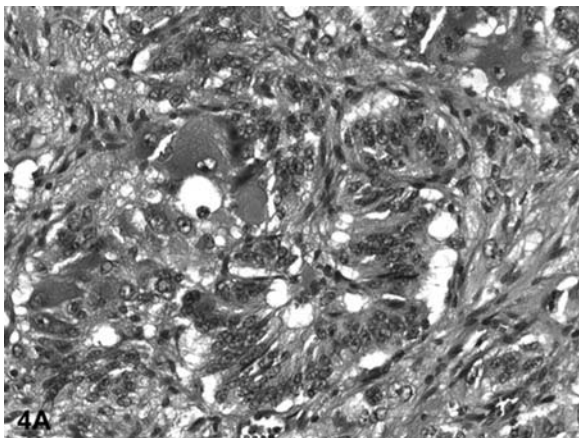
**Purpose:** Gangliocytic paraganglioma (GP) is a rare neoplasm of uncertain histogenesis that typically occurs in adults in the second portion of the duodenum. We report the first two cases describing the cytologic features of GP diagnosed using fine-needle aspiration biopsy (FNAB).

**Methods:** Case 1 was a 43 year-old Caucasian man with an 8.5 cm intraluminal, submucosal mass in the second portion of the duodenum adjacent to the ampulla of Vater. Endoscopic ultrasound-guided FNAB was diagnosed as a GP and confirmed in the subsequent resection specimen. Case 2 was a 67 year-old Caucasian man with a 2.5 cm submucosal mass in the second portion of the duodenum adjacent to the ampulla of Vater. An intra-operative FNAB was diagnosed as a spindle cell neoplasm and the resection specimen was diagnosed as a GP.



**Results:** FNAB smears demonstrated a combination of three distinct cell types: ganglion cells, epithelioid cells, and spindle cells (Fig. 2A). Both resection specimens demonstrated submucosal neoplasms also composed of these three cell components (Fig. 4A). Immunohistochemical staining results from the resection specimens included: ganglion cells immunoreactive for synaptophysin; epithelioid cells immunoreactive for synaptophysin [also immunoreactive for somatostatin in Case 1]; and spindle cells immunoreactive for S100 protein.

**Conclusion:** In the appropriate clinical and radiographic context, an FNAB exhibiting ganglion cells, epithelioid cells, and spindle cells is characteristic of GP.[figure1][figure2]



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#### Continuous Intravenous Administration of Teduglutide (ALX-0600), a Glucagon-like Peptide-2 (GLP-2) Analog Induces Intestinotrophic Activity

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**Purpose:** Teduglutide is an analog of human GLP-2, a naturally occurring peptide secreted from endocrine L cells predominantly in the distal intestine. Teduglutide has been shown to increase intestinal mass as a result of increased villus height and crypt depth. In preclinical rodent models, subcutaneous administration of teduglutide augments the adaptive response following small bowel resection and reduces the deleterious effects of IBD-related and chemotherapy-induced intestinal damage. This study compared the intestinotrophic effects of continuous intravenous to daily subcutaneous administration of teduglutide in rat.

**Methods:** Female Sprague Dawley rats were administered teduglutide either by continuous intravenous infusion (0.5 mg/kg/day) or subcutaneous injection (0.5 mg/kg/day, b.i.d.) for 14 days. Morphological changes, including intestinal weight and length, were used to measure changes in the gastrointestinal tract.

**Results:** Small and large intestinal weights increased significantly, by 125% and 35% respectively, in animals treated with teduglutide by continuous infusion. Small intestinal weight increased significantly by 88% and a trend towards increased large intestinal weight was observed in animals receiving teduglutide by subcutaneous injection. A trend towards increased small intestinal length was observed in both treatment groups, however, this effect only reached statistical significance in animals administered teduglutide by continuous infusion. Increased villus height was observed in the small intestine in animals given teduglutide intravenously and in the small and large intestine in animals given teduglutide subcutaneously. The pharmacokinetics following intravenous infusion of teduglutide were predictable and the steady-state plasma concentration of teduglutide was maintained throughout

the 14 days of dosing ( $40.2 \pm 8.8$  ng/mL on Day 2 and  $50 \pm 30.8$  ng/mL on Day 14). The total daily exposure to teduglutide was higher in the intravenous group (965–1200 ng-h/mL) than in the group receiving the same dose of teduglutide by subcutaneous injection (682 ng-h/mL).

**Conclusion:** Administration of teduglutide by continuous intravenous infusion or subcutaneous injection was associated with increased intestinal weights and intestinal mucosal mass. Plasma concentrations after continuous intravenous infusion of teduglutide were well predicted. These results suggest that continuous systemic and intermittent exposure to teduglutide give similar pharmacological responses.

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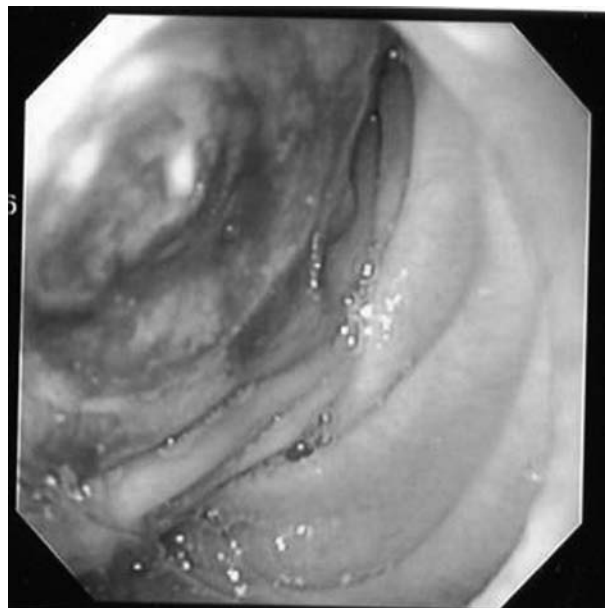
#### Primary Aortoduodenal Fistula Caused by Mycobacterium Avium Complex

Pallavi K. Rao, MD, Kanan Sharma, MD, Christopher Barde, MD\*.

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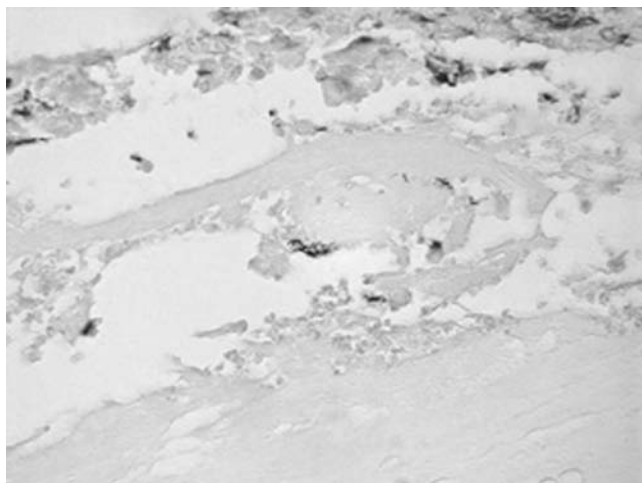
**Purpose:** A 48 year-old man with history of HIV infection, CD4 count of 138, on HAART, presented with recurrent episodes of hematemesis and hematochezia. He was afebrile, hypotensive and tachycardic. The laboratory values were normal except for WBC count of 14,000 and hemoglobin 12.9. A large 3–4 cm duodenal ulcer with blood clot was seen on emergent EGD. An abdominal CT scan revealed aortoduodenal fistula in third portion of the duodenum and ruptured aortic abdominal aneurysm (AAA). An emergent surgery for AAA was performed with repair of the duodenum. The surgical specimen of the aortoduodenal fistula was positive for acid-fast bacilli on ziehl-neelsen stain. Histology showed scattered non-caseating granulomas, chronic inflammation and scattered foci of acid-fast bacillary organisms, which exhibit a beaded microscopic appearance. This morphology was consistent with MAC. Blood cultures for acid-fast bacilli were negative for 6 weeks period. He was initially treated with intravenous azithromycin, rifampin and levofloxacin for MAC. Upon discharge he was switched to azithromycin, rifabutin and ethambutol.

**Discussion:** Primary aortoduodenal fistula is a rare cause of massive upper gastrointestinal bleeding. It occurs as a result of spontaneous connection between the aorta and the third or fourth portion of the duodenum. The reported incidence of primary aortoenteric fistula is about 0.07% in the general population from a large autopsy series. There are reports of fistula occurring





due to infection, tumor, radiotherapy and foreign body ingestion. Reported infectious causes of primary aortoenteric fistula are *Escherichia coli*, *Enterococcus faecalis*, *salmonella*, *Mycobacterium tuberculosis*, *Clostridium septicum*, *Lactobacillus* and *Klebsiella*. We report the first case of MAC as a cause of primary aortoduodenal fistula causing massive upper gastrointestinal bleeding.[figure1][figure2]



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### Positive Predictive Value of Tissue Transglutaminase: A Retrospective Review at Our Institution

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**Purpose:** To determine: 1) the positive predictive value (PPV) of the IgA tissue transglutaminase (tTG) assay for celiac disease (CD), with variable clinical indications for ordering the test; 2) the PPV of the tTG titer; and 3) the correlation of tTG titer with small bowel histology.

**Methods:** A retrospective analysis of positive tTG titers from 99 patients, representing all positive assays at our institution from 2002–2006, for whom we had concurrent histologic data. Our lab utilizes the human tTG IgA, with a positive result at >20 units.

**Results:** The PPV of tTG for biopsy-confirmed CD in patients with:

1. Overall clinical indications listed below, was 78.8% (78/99).
2. Diarrhea with and without iron-deficiency anemia (IDA), was 68% (17/25).
  - 2a. Diarrhea and IDA, was 71.4% (5/7).
  - 2b. Diarrhea without IDA, was 66.7% (12/18).
3. IDA without diarrhea, was 66.7% (6/9).
4. Non-specific malabsorptive symptoms, weight loss, or failure to thrive, was 83.3% (15/18).
5. Non-specific gastrointestinal complaints (e.g., abdominal pain, constipation), was 69.2% (18/26).
6. Abnormal liver enzymes and negative standard serologic evaluations for primary liver disease, was 87.5% (7/8).
7. Unexpected endoscopic findings consistent with CD, was 100% (7/7).

The threshold level at which:

- a. 100% of patients had CD was 158.7 units.
- b. 95% of patients had CD was 99.6 units.
- c. 90% of patients had CD was 41.0 units.
- d. 80% of patients had CD was 26.6 units.

The mean tTG level for patients with positive tTG tests and:

- i. normal small bowel biopsies was 41.5 units.
- ii. biopsies revealing increased intra-epithelial lymphocytes and/or crypt hyperplasia without villous atrophy (Marsh I and II) was 38.6 units.
- iii. biopsies revealing partial villous atrophy (Marsh III) was 106.2 units.
- iv. biopsies revealing total villous atrophy (Marsh IV) was 156.7 units.

**Conclusion:** The positive predictive value of the tTG assay for celiac disease was unexpectedly robust when applied to scenarios of non-screening, case-finding by clinical indications, varying from 66.7% – 87.5% depending on the indication. A high PPV of 90% is achieved at a relatively low titer of 41 units. Although there was a correlation between the titer of tTG and the severity of CD histologic findings on small bowel biopsies, there was no significant difference in average titer between normal biopsies and Marsh I and II lesions (infiltrative without villous atrophy).

## 253

### Disparity in Gastroenterology: Is It Just “ACADEMIC” or a Significant Problem? A 10 Year Prospective Cohort Study

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**Purpose:** Our previous data demonstrated disparity in income, family and practice patterns between men and women in GI. We sought to identify disparities between Private (PP) and Academic practice (AP) or between men & women within these practice types, 10 years after fellowship.

**Methods:** A 36-question survey was sent originally to a cohort of 390 GI fellows at the time of graduation, and 3, 5 and 10 yr later. We herein analyzed yr-10 data for practice and gender differences using t-test for continuous, chi square for categorical variables and linear regression for adjusted income.

**Results:** 171 individuals (149 men, 22 women) responded. 77% are in PP and 23% in AP. 81% of men and 50% of women are in PP.

PP vs AP: Compared to PP, academicians were more often married to a physician (44% vs 22%,  $P = 0.01$ ) and childless (13% vs 1.5%,  $P = 0.01$ ). Respondents in PP worked less hrs/wk but made significantly higher income than those in AP.

Table 1. PP vs AP

	PP	AP	P-value
Mean income/yr	391K	253K	<0.001
Dollars/hr income	148	90	<0.001
Work hrs/wk	52	56	0.04
Call days/month	9	5	<0.001
Vacation wks/yr	5	4	0.07
CME days/yr	6	9	<0.01

Gender Disparity in PP vs AP: In both PP and AP women's annual income was lower than men's. In PP women work less hrs/wk, take less call-days and more vacation than men. However, in AP, no significant difference in work-hr or vacation time was noted between men and women.

Multivariate analysis adjusting for work hrs, vacation time, call days and practice ownership shows the annual income of women is \$100K less than men in AP ( $P = 0.003$ ), and \$60K less in PP ( $P = 0.08$ ).

**Conclusion:** Gastroenterologists in AP work longer hours but get paid significantly less than those in PP. Significant disparities in earnings and family structure exist for women in both PP and AP. While a greater proportion of women than men are in AP the disparity in income is greatest for women in that practice setting. Recognition of these disparities is imperative and steps to minimize these in both AP and PP are warranted.

Table 2. Gender Disparity: PP vs AP

	PP			AP		
	Male (N = 121)	Female (N = 11)	P-value	Male (N = 28)	Female (N = 11)	P-value
Mean income/yr	399K	317K	0.04	282K	179K	0.04
Dollars/hr income	149	142	0.59	97	75	0.09
Work hrs/wk	53	43	<0.01	58	52	0.19
Call days/month	9.7	4.8	0.02	5.4	4.4	0.51
Vacation wks/yr	4.9	8.1	<0.01	4.1	4.2	0.63

## 254

**The Yield of Routine Endoscopy with Duodenal Biopsies To Exclude Celiac Disease**

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**Purpose:** Celiac disease is an autoimmune condition that has classically been defined as a malabsorption syndrome with symptoms of chronic diarrhea, steatorrhea, abdominal bloating, edema and weakness. However, today, it is now recognized that there are many "atypical" signs and symptoms which include dyspepsia, vomiting, reflux, osteopenia, iron deficiency anemia, infertility, and peripheral neuropathy. Many patients will undergo endoscopic evaluation specifically for the purpose of obtaining duodenal biopsy to rule out celiac disease. The purpose of this study is to investigate the yield of routine biopsies as well as the cost per case diagnosed in patients whom celiac sprue is suspected.

**Methods:** Patients who had duodenal biopsies taken from January 1, 2004 to December 31, 2005 at Cleveland Clinic Florida were retrospectively identified. Patients were selected for the study if they had duodenal biopsies taken to rule out celiac sprue per written instruction from the gastroenterologist performing the procedure to the pathologist. The medical chart of these patients were carefully reviewed with notice to the clinical history, indication for the endoscopy, appearance of the duodenum, number of biopsies taken, as well as pathologic findings. Cost-effectiveness ratio was calculated for each procedure based on Medicare reimbursement from 2006.

**Results:** A total of 273 patients met the criteria for the study. A positive diagnosis of celiac disease was made in 7 individuals for a yield of 2.57%. In patients with classic symptoms of celiac disease, 6 out of 23 patients were found to have celiac disease for a yield of 26.08% with a cost-effectiveness of \$3021 per case diagnosed. In atypical patients, only 1 out of 250 patients were found to have celiac disease for a yield of 0.40% and a cost-effectiveness of \$197,000 per case. Nineteen patients were found to have stigmata of celiac disease in the duodenum on endoscopic examination. Six were found to be positive for celiac disease. The sensitivity of endoscopic stigmata was found to be 87.5% and the specificity was 95.1%. The positive predictive value was 35.0% with a negative predictive value of 99.6%.

**Conclusion:** Many patients who may have celiac disease will undergo upper endoscopy specifically for the purpose of obtaining a duodenal biopsy specimen to rule out the disease. Due to the low yield and high cost per case diagnosed in atypical patients, serologic screening may be a better initial approach.

## 255

**Clinical Characteristics and Prevalence of Celiac Disease and Non-Celiac Gluten Sensitivity Presenting to a Community Based Private Gastroenterology Clinic**

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**Purpose:** The prevalence and clinical features of Celiac disease (CD) and Non-celiac gluten sensitivity in a community based gastroenterology practice is reviewed.

**Methods:** The records of all patients with suspected CD presenting to a private practice gastroenterologist were reviewed. Comprehensive celiac disease panel requested on all patients consisted of total serum IgA level, anti-gliadin (AGA) IgA and IgG, endomysial IgA (EMA) and tissue transglutaminase (TTG) IgA antibodies.

Patients presenting for diagnostic upper endoscopy and GI consultation for symptoms were screened for CD. Those presenting for routine screening and surveillance colonoscopy with identifiable risk factors for CD were offered screening. CD was defined using standard criteria.

**Results:** Records of 367 patients were reviewed. Women outnumbered men by ratio of 2.8:1 overall but the ratio narrowed to 1.4:1 in patients with CD and was confirmed in 12.5%. HLA DQ results were obtained in 69% of patients, 55% of whom were DQ2 positive and 22% DQ8 positive. All with a positive EMA and TTG in whom DQ was known were positive for DQ2 and/or DQ8 and met criteria for CD. The prevalence of IgA deficiency was 4% overall but 13% in CD.

The average intraepithelial lymphocyte count per 100 epithelial cells was 47 in CD. Those failing to meet strict criteria for CD, but believed to be gluten sensitive based on clinical presentation and response to gluten free diet had on average 23 IELs/100 epithelial cells.

**Conclusion:** The estimated prevalence of CD in the general population of 1% probably significantly underestimates that of patients presenting to a general gastroenterology practice. Because more than 10% of people with CD are IgA deficient total serum IgA levels should be checked on all patients suspected of CD to avoid false negative EMA and TTG IgA tests. AGA tests, though not specific for CD, may identify patients with elevated IELs, villous blunting and favorable response to a GF diet. If either EMA or TTG are positive, DQ2 or DQ8 is likely present. Higher IEL counts are more often found in CD however, the presence of elevated AGA and IEL counts in the range of 20–25 are more common in patients failing to meet strict criteria for CD but who may respond to a gluten free diet, the so-called non-celiac gluten sensitive (NCGS).

## 256

**Double Balloon Enteroscopy: Virginia Commonwealth University Health System Experience**

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**Purpose:** Review the initial experience with a double-balloon enteroscopy at VCUHS.

**Methods:** This was a retrospective review of the first 100 DBE procedures performed at our center between August 2004 and June 2007 using the Fujinon EN-405T5.

**Results:** 100 DBE procedures were performed on 86 patients. 83 DBE were antegrade (per-oral) and 17 retrograde (per-anal). 85 DBEs were performed using conscious sedation and 15 were done under general anesthesia. The most common indication was obscure GI bleeding (overt and occult) as seen in 88% of patients. Other indications included abdominal pain (5%), tumor/polyps (5%), and retained capsule (2%). Mean procedure time 83 minutes (range 25–210). The first 37 DBEs were performed with fluoroscopy.

The remaining DBEs were done without fluoroscopy. Complete enteroscopy was not possible in all patients despite a combined antegrade and retrograde approach. In 8 patients the procedure could not be completed (6 due to inability to tolerate the conscious sedation and 2 due to inability to advance the scope through the ileocecal valve for a retrograde DBE). There were no major complications. All patients were discharged from the endoscopy suite after a 2 hour recovery period. Findings were seen in 61% of the DBEs performed. In 39% of the cases the DBE exam was normal. Of those with positive findings (N = 61) AVM were seen in 63%, erosions or ulcers seen in 13%, Dieulafoy lesions in 4%, polyps in 2%. One patient had a stricture and ulceration; biopsies demonstrated lymphoma. No other case of malignancy was found. In 40% APC treatment was performed. Biopsies were performed in 12% of all DBE, clip and injection in 5%, dilation of a stricture done in 1%. Tattooing to help locate a lesion in the small intestine for laparoscopic treatment was performed in 2%. Tattooing to mark the most distal part of the small intestine reached, was performed in 79% of cases.

**Conclusion:** DBE is safe and provides positive findings in the majority of the cases. AVM is the most commonly found lesions. Therapeutic applications can be frequently performed (APC, biopsies, injection, clip, dilation and tattooing). While time consuming, this technique allows the diagnosis and treatment of lesions in the small bowel. In few cases despite combined antegrade and retrograde attempt to examine the entire length of the small bowel, this was unsuccessful.

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### Liver and Gastrointestinal Manifestations of Dengue Hemorrhagic Fever. An Analysis from a Cohort of 263 Hospitalized Patients

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**Purpose:** Dengue fever result from infection with any of the 4 dengue virus serotypes (DEN 1–4). Clinical manifestations range from a mild, flulike and self-limited febrile illness to severe illness with hemorrhage (DHF). Although, liver abnormalities have been described as a manifestation of DHF, the prevalence of other gastrointestinal manifestations is unknown. Our aim was to evaluate the prevalence of liver and gastrointestinal involvement in a cohort of patients with DHF.

**Methods:** Dengue fever is an endemic diseases in the state of Veracruz, Mexico. We retrospectively review clinical charts from 9005 subjects who suffered dengue fever in the 2006 epidemic. Patients who where hospitalized because of DHF, at the Veracruz Regional Hospital were included for analysis. The diagnosis of DHF was based on serological positive test and manifestations. Demographic data, clinical manifestations, laboratory data (peripheral white blood cell count, platelet count, prothrombin time, activated partial thromboplastin time, aspartate and alanine aminotransferase levels, hematocrit, and serum creatinine), and clinical course and outcomes were obtained from the medical records for analyses.

**Results:** Among 9005 patients, 263 were hospitalized. Fortyfive percent were female and 55% were male. Mean age was 30.3 years (range 5–74) Seventyone patients (27%) had some form of gastrointestinal man-

ifestation. Fifty of the 71 patients (70%) had abnormal aminotransferases (ALT and/or AST) during the course of their disease. Four patients (6%) had a direct bilirubin greater than 0.8 mg/dL. All the patients with gastrointestinal manifestations had less than 105,000 platelets. Thirty-nine (55%) and 37(52%) had nausea and vomiting respectively. One patient developed acute pancreatitis. Six patient had gastrointestinal bleeding of which 5 had upper GI source and 1 patient had lower GI bleeding. Mean hospital stay was 4.5 days (range 1–14). There were no deaths.

**Conclusion:** Most patients with DHF had liver abnormalities. Up to 50% of the patients had other GI manifestations such as nausea, vomiting, or GI bleeding. Our findings suggest that in patients with acute fever syndrome with abnormal liver function tests and GI manifestations, living in an endemic area, Dengue fever should be suspected.

## 258

### Pharmacokinetics and Safety Profile of a Range of Teduglutide Doses Given for Eight Days in Healthy Volunteers

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**Purpose:** Data from animal and human studies indicate that both GLP-2 and teduglutide (TD) stimulate the growth and proliferation of intestinal epithelial cells. The **goal** of this study was to investigate the pharmacokinetics (PK), and safety and tolerability of a range of doses of TD or volume matched placebo (PL) in healthy volunteers over an eight day period.

**Methods:** A Phase 1 single-center, double-blinded, randomized, placebo-controlled study enrolled 96 healthy volunteers. Seventy two volunteers received doses of 10, 15, 20, 25, 30, 50 or 80 mg TD and 23 received PL as a subcutaneous injection for eight consecutive days with a follow-up visit seven days after the last dose.

**Results:** There were 302 adverse events (296 mild, 5 moderate, and 1 severe). Most frequent were gastrointestinal, 94 in the 72 TD subjects and 25 in the 23 PL subjects, followed by injection site reactions (86 for TD and 19 for PL). Six subjects withdrew consent (2 on PL, 1 on TD), one withdrew due to severe adverse event (PL, vasovagal syncope), 2 TD for other reasons. Eight subjects receiving doses of 15, 20 or 30 mg of TD showed mild elevations of AST and ALT enzymes by Day 4 of dosing. (defined by FDA guidance to be less than 2.5 times the upper limit of normal). Among these eight subjects, seven subjects' liver enzyme levels returned to normal by the follow up visit (within 7 days after the last dose), and the other subject's liver enzyme level returned to normal within 2 weeks of the last dose. No dose response in elevated LFTs was observed and none of the subjects receiving the highest doses of 50 and 80 mg showed elevated LFTs. PK parameters of the 20 and 80 mg/d dose cohorts follow. [Teduglutide Pharmacokinetics]

**Conclusion:** Teduglutide appears to be safe in humans for short-term treatment in doses exceeding up to 10 to 4 respectively times the highest dose applied in current clinical trials involving patients with short bowel syndrome and Crohn's disease. Mild and reversible changes in liver enzyme levels are possibly associated with exposure to teduglutide or other factors such as confinement in a Phase 1 clinic in a dose-independent manner. The PK of teduglutide is predictable and consistent.

**Table 1.** Teduglutide Pharmacokinetics

Teduglutide 20 mg/day sc				Teduglutide 80 mg/day sc			
AUC (ng.hr/ml)	Cmax (ng/ml)	tmax (hr)	t1/2 (hr)	AUC (ng.hr/ml)	Cmax (ng/ml)	tmax (hr)	t1/2 (hr)
Day 1 1781.0	284.2	3.2	2.4	5112.6	562.1	6.5	5.4
Day 2 1688.4	280.8	3.5	2.8	5088.4	554.5	4.5	4.5

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### The Significance of Antineutrophil Cytoplasmic Antibody in Adult Patients with Henoch-Schönlein Purpura Presenting Mainly with Gastrointestinal Symptoms

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**Purpose:** This study is to test the clinical significance of ANCA in evaluation of adult HSP patients presenting mainly with abdominal symptoms.

**Methods:** Twenty eight consecutive Henoch-Schönlein purpura (HSP) patients who presented predominantly with abdominal symptoms were enrolled in this study. Control subjects included 27 age and sex-matched patients with peptic ulcer disease, colon cancer, acute gastroenteritis, irritable bowel syndrome and colonic polyps. ANCA were measured by indirect immunofluorescence (IIF) in all patients; and follow-up ELISA assay was performed in patients with positive IIF tests.

**Results:** ANCA was detected in 9 HSP patients by IIF (2 positive for c-ANCA and 7 positive for p-ANCA). No ANCA was found in the control group. The sensitivity and specificity of a positive ANCA test (either c- or p-ANCA) was 32.1% and 100% respectively. Among the 9 patients with positive ANCA by IIF, only one was positive by ELISA and the antigen was myeloperoxidase (MPO). The patients with ANCA positivity had higher HSP clinical scores, and were more likely to have renal function impairment (table 1).

**Conclusion:** ANCA is not a sensitive but a specific marker for adult HSP who presented predominantly with abdominal symptoms. A positive ANCA test is associated with more severe symptoms.

**Table 1.** Blood Creatine and 24-hours Urinary Protein in HSP Patients

	Blood creatine ( $\mu\text{mol/L}$ )	24-hours urinary protein (g/L)
ANCA(+)	320 $\pm$ 22 (3.64 $\pm$ 0.25 mg/dl)	1.78 $\pm$ 0.12
ANCA(-)	104 $\pm$ 15* (1.19 $\pm$ 0.16 mg/dl)	0.78 $\pm$ 0.32*

\*P < 0.05 ANCA (+) HSP patients vs. ANCA (-) HSP patients

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### Kaposi's Sarcoma Presenting as Small Bowel Intussusception: Case Presentation and Review of the Literature

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**Purpose:** KS was rarely seen in the US before the start of transplant medicine and the HIV epidemic. Bowel intussusception is common in children but represents only 1% of cases in adults. Unlike children, adult intussusception is associated with pathological lesions. In HIV patients the most frequent GI tumor is KS. However most cases are asymptomatic. Few cases of KS presenting with intussusception are described in the literature. We present KS of the small intestine associated with intussusception in an HIV positive adult.

**Case Scenario:** A 37 year old homosexual male, HIV positive, presented with non-radiating sharp abdominal pain associated with vomiting and non-bloody watery diarrhea. He was non-compliant with HAART.

On exam he was afebrile. Abdomen was soft, diffusely tender. Bowel sounds were audible. Stool guaiac was negative.

Abdominal X-ray showed multiple air fluid levels suggestive of small bowel obstruction. Abdominal CT showed ileo-ileal intussusception resulting in small bowel obstruction. At laparotomy he had telescoping of ileum (intussusception). Affected portion of small bowel was removed. Biopsy showed KS. Recovery was uneventful.

**Discussion:** In AIDS patients, KS is the most frequent tumor of the GI tract. It has been reported throughout the GI tract, including the oropharynx, esophagus, stomach, small and large intestines, anus, liver, spleen and pancreas. 50% of cases involve the oral mucosa. It usually remains asymptomatic. In AIDS patients, on autopsy, KS involved the abdominal viscera in 77% of cases. In symptomatic cases, it manifested as GI bleeding, intestinal obstruction, intussusception, perforation and protein losing enteropathy. In the literature we found 9 cases of KS presenting as intussusceptions in patients with AIDS (see table). Most of the cases involve the small bowel. 50% had skin involvement. Our case illustrates this life threatening but rare manifestation of a commonly occurring disease in HIV patients. KS should be considered in the differential diagnosis of an acute abdomen in AIDS patients.

Published cases of KS intussusception

AUTHOR/YEAR	HIV POSITIVE	AREA OF GI INVOLVED	SKIN MANIFESTATION
Tedeschi 1947	x	Small Bowel	Unknown
White 1964	x	Colon	Unknown
Birch 1967	x	Jejunum-ileum	No
Coetzee 1967	x	Small Bowel	Yes
Khorshid 1987	Yes	Ileum	Yes
Khorshid 1987	Unknown	Small Bowel	No
Hofstetter 1988	Yes	Jejunum	Yes
Gulick 1997	Yes	Small Bowel	Yes
Wang 2002	Yes	Ileum	No
This Report	Yes	Small Bowel	No

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### Revisiting Capsule Endoscopy in the Diagnosis of Small Bowel Malignancy

Anthony Aghenta, MD, Ayodele Osoyo, MD, Tarun Kothari, MD, FACG, FACP\*. Internal Medicine, Unity Health System, Rochester, NY.

**Purpose:** Small bowel malignancy is rare but the diagnostic modalities for small bowel pathologies in the pre-capsule endoscopy (CE) era were limited resulting in delayed diagnosis and poor prognosis for malignant tumors. In evaluating obscure GI bleed recent studies have shown the superiority of CE in the detection of small bowel tumors.

**Case 1:** A 74 year old white male presented with a history of GERD and persistent iron deficiency anemia despite iron therapy and blood transfusions. FOBT was negative. Tests revealed a Hct of 26.4%, Hgb of 8.1 gm/dl, MCV 88.4fl, platelet count 423,000/cumm, serum iron 14 mcg/dl, TIBC 440 mcg/dl, ferritin 4 mcg/l, and transferrin saturation 3%. EGD, CT scan of the abdomen and colonoscopy were unremarkable. CE showed an ulcerated bleeding stricture in the mid ileal region. He underwent laparotomy with bowel resection. Histology confirmed adenocarcinoma.

**Case 2:** A 75 year old white female with history of chronic abdominal pain and iron deficiency anemia presented with hematocrit of 26.2 and MCV of 66.1. FOBTs were negative. Over the preceding 4 years she had several tests done including 2 abdominal CT Scans, 2 EGDs, SBFT, and colonoscopy. She remained iron deficient despite iron therapy and blood transfusion. CE showed bleeding in the distal ileum, intra-operative enteroscopy then revealed a bleeding mass in the distal jejunum that was resected. Histology confirmed small bowel adenocarcinoma.

**Case 3:** A 55 year old white male with history of iron deficiency anemia on iron therapy initially diagnosed 2 years prior presented with fatigue, palpitations, and shortness of breath. His hematocrit was 19.9, with MCV of 69.2. FOBT was negative. EGD and colonoscopy were unremarkable. CE was unremarkable but push enteroscopy revealed fresh blood and organized blood clot in the proximal jejunum. CT scan of the abdomen showed 4 hypodense lesions in the liver. He underwent laparoscopic exploration with segmental resection of the jejunum and wedge biopsy of the liver lesions.

Histology confirmed gastrointestinal stromal tumor (GIST) with metastasis to the liver.

**Conclusion:** In the course of iron deficiency anemia, GI bleeding may not be detected by FOBT even when multiple tests are done. Case 1 and 2 highlight the utility of CE in diagnosing small bowel malignancy. Case 3 however attenuates the infallibility of CE. Although only a few studies have reported clinically significant lesions identified by enteroscopy but missed by CE, both test modalities are better optimized when complemented.

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### Nitazoxanide for the Treatment of SIBO-Related Gastrointestinal Symptoms

Harry Moulis, MD\*, Gregory J. Stella, MD, Louis M. Agnone, MD, Donato R. Ricci, MD, Sunil P. Pasricha, MD, David B. Mostellar, PharmD. Gastrointestinal Associates, P.A., Port Orange, FL and Department of Medical Science, Romark Laboratories, L.C., Tampa, FL.

**Purpose:** Small intestinal bacterial overgrowth (SIBO) is a clinical condition defined as an abnormally high bacterial population in the small intestine. SIBO symptoms are variable, with abdominal pain or discomfort, bloating, diarrhea, and flatulence being the most common. Nitazoxanide (NTZ) is a first in class thiazolide antibiotic with a targeted anaerobic antibacterial activity, placebo-like safety profile, and high gastrointestinal (GI) concentration. To date no studies have evaluated the empiric use of NTZ for the treatment of GI related symptoms in SIBO patients. The purpose of this paper is to report on practice experience utilizing NTZ for the treatment of SIBO-related GI symptoms in a community setting.

**Methods:** A chart review was performed on eleven consecutive patients treated with NTZ for the diagnosis of SIBO. The diagnosis of SIBO was made by the attending physician based on the patient's symptoms and positive lactulose breath test. Patients meeting this criteria were prescribed NTZ 500 mg twice daily for five days. Efficacy was measured as resolution of the patient's GI related symptoms 2–4 weeks after the end of therapy; repeat lactulose breath tests were not performed. The primary markers for resolution included: abdominal pain, diarrhea, bloating, and/or flatulence.

**Results:** Of the eleven patients treated with NTZ, seven were available for follow-up evaluation. The four remaining patients have not returned to the clinic with any GI related complaints. A complete resolution of symptoms was reported in five out of the seven patients treated with NTZ. Of the two patients that did not respond to therapy, one patient was not able to tolerate the medication due to an unknown reason. The other nonresponder had failed multiple previous regimens including antibiotics, probiotics, and pancreatic enzymes. Table one summarizes patient responses to NTZ therapy.

**Conclusion:** The empiric use of nitazoxanide 500 mg twice daily appears to be a safe and effective therapy for the treatment of SIBO-related GI symptoms. To further support these findings, larger controlled clinical trials are warranted.

Table 1.

symptom	resolved or improved	No change/Worsen
Diarrhea	5/6 (83%)	1/6 (17%)
Bloating	3/5 (60%)	2/5 (40%)
Abdominal pain	2/2 (100%)	N/A
Flatulence	1/1	N/A

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### Enteroscopy Using the New 47F Discovery SB and Fujinon Enteroscope

Paul A. Akerman, MD\*, Daniel Cantero, MD, Jose Avila, MD. University Gastroenterology, Providence, RI; Hospital Francais, Ascuncion, Paraguay and Rhode Island Hospital, Providence, RI.

**Purpose:** All methods of small bowel enteroscopy have significant limitations. The Discovery SB has been shown to work with the pediatric colonoscope. Reduced size (58 F to 47 F) and increased length of the enteroscope may have significant advantages for deep small bowel insertion with minimal mucosal damage. The Discovery SB overtube and enteroscope work by using a rotating raised spiral to pleat small bowel. This pilot study is to evaluate the new Discovery SB and Fujinon 9.4 mm enteroscope.

**Methods:** The new Discovery SB overtube is 47 F, 118 cm long with a 5 mm raised spiral 21 cm long at the distal end. There is a locking collar that allows spiral pleating or unlocking for push advancement and gathering small bowel. Indications for the procedure were obscure bleeding or abnormal imaging studies. Enteroscopy was performed in 7 patients by two endoscopists. Informed consent was obtained. Propofol, Fentanyl and Versed were used for sedation. The new 47 F Discovery SB was placed over the Fujinon 9.4 mm 200 cm enteroscope and both were advanced with gentle push and rotation past the Ligament of Treitz (LOT). Once past the LOT the Discovery SB was rotated and pleating of small bowel was achieved. Further advancement was achieved with unlocking the Discovery SB and pushing the enteroscope through the overtube. The Discovery SB was then rotationally advanced over the enteroscope and the process repeated. Withdrawal was achieved with anticlockwise rotation of the overtube. Depth of insertion was determined by endoscopic criteria.

**Results:** Enteroscopy with spiral advancement was completed in all 7 patients, 3 M, 4 F. Average age was 47 yrs, average weight/height was 165 cm/70 kg. Average sedation was 80 mg Propofol, 4.5 mg Versed and 90 mcg Fentanyl. All patients tolerated the procedures well. There were no complications. Minimal mucosa trauma was seen in 2 patients. 2 patients had AVM's. 1 patient a small bowel adenocarcinoma. Average depth of insertion past the LOT was estimated to be 202 cm (Range 60–380 cm) Deepest insertion depth was proximal ileum. Average total time of procedure was 34.5 minutes (Range 21–55 minutes).

**Conclusion:** The new 47 F Discovery SB and Fujinon 9.4 mm enteroscope is safe and effective for rapid advancement through the small bowel. Deep small bowel intubation can be achieved by spiralling the new Discovery SB and pleating small bowel.

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### Magnetic Resonance Imaging (MRI) of the Small Intestine: Utility of This Modality in a Large Urban Community Hospital

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**Purpose:** Evaluation of the small bowel is difficult. Current modalities include computed tomography scan, capsule endoscopy, enteroscopy, enteroclysis, angiography, small bowel follow through, and surgery. However, each technique has limitations. Small bowel MRI is an efficient and tolerable technique with limited availability nationally. This technique is not invasive, does not involve radiation, and provides detailed information regarding mucosal and transmural inflammation and wall thickness. The purpose of this study is to determine the application of small bowel MRI in a large urban community teaching hospital.

**Methods:** Small bowel MRI with gadolinium involves administration of psyllium fiber as an intraluminal agent taken in advance over a 3 hour period, and the use of glucagon during the examination. This is a retrospective chart review to determine the indications, results, therapy, and management for 40 patients undergoing small bowel MRI at a large urban community teaching hospital from January 2006 to January 2007.

**Results:** Indications for small bowel MRI included abdominal pain (22 patients), suspected Crohn's disease (12 patients), anemia (3 patients), gastrointestinal bleed (1 patient), and abnormal CT abdomen (2 patients). Small bowel MRI was abnormal in 14 patients: small bowel thickening (8 patients), stricture (3 patients), and small bowel obstruction (3 patients). In 17 patients there had been previous small bowel imaging including capsule endoscopy,

CT abdomen, small bowel follow through, and abdominal x-ray. In 9 patients with abnormal findings on a prior study, MRI confirmed the finding in 5 patients but changed the diagnosis in 4. As a result, 2 patients averted surgery; 2 patients no longer were given a diagnosis of Crohn's disease. MRI did confirm normal small bowel imaging in 8 patients.

**Conclusion:** Small bowel MRI did confirm normal results in 8 patient with prior imaging, and more importantly, it did identify false positive results in 4 out of 17 patients with prior imaging. The identification of false positive results altered patient management. Small bowel MRI is a noninvasive tool which utilizes an inexpensive and tolerable intraluminal agent, requires no radiation, and provides detailed imaging. Therefore, small bowel MRI should be considered for evaluation of the small bowel in large community hospitals.

## 265

### Mantle Cell Lymphoma of the GI Tract: Is It Distinctive from Other Gastrointestinal Lymphomas?

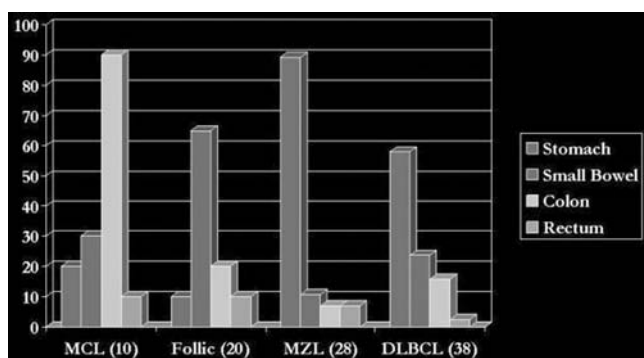
Adrianne LaJoie, MD\*, Williamson B. Strum, MD. Gastroenterology and Hepatology, Scripps Clinic and Research Institute, La Jolla, CA.

**Purpose:** Mantle cell lymphoma (MCL) is a relatively new subtype of B-cell lymphoma that involves the GI tract in up to 88% of patients. MCL is distinguished by overexpression of the cyclin D1 protein which promotes cell division, and mucosal affinity for the alpha-4-beta-7 receptor. Our aim was to examine the clinicopathologic features of MCL compared to follicular (FL), marginal zone lymphoma of MALT type (MZL) and diffuse large B-cell lymphoma (DLBCL). We tested the null hypothesis that there is no difference in site of involvement between MCL and other GI lymphomas.

**Methods:** Cases of gastrointestinal lymphoma were collected from five community hospitals in San Diego and identified by histology and flow cytometry. Age, gender, clinical presentation, site of involvement, endoscopic appearance, and bone marrow involvement were analyzed.

**Results:** A total of 96 cases were reviewed and included (MCL = 10, FL = 20, MZL = 28, DLBCL = 38). Median age at presentation was similar (age range 28–97; median age 62–68). 70% of MCL patients were men. Endoscopic appearances varied from multiple small nodules to large polypoid lesions to ulcerated masses. There were no characteristic endoscopic findings for any lymphoma type. Compared to patients with FL, MZL and DLBCL, patients with MCL had significantly more colonic involvement ( $P < 0.001$ ) and were more likely to present with stage IV disease ( $P < 0.02-0.001$ ). Greater than 85% of MCL patients were positive for cyclin D1. MZL and DLBCL were more likely to present with GI bleeding (14.3% and 10.5%, respectively), while no patients with FL or MCL bled. While 25% of patients with FL presented with small bowel obstruction, no patients with MCL had this presentation. These data disprove the null hypothesis.

**Conclusion:** Clinical markers are available to distinguish MCL from other lymphomas. Age, sex, and endoscopic appearance are overlapping and not distinctive. The most helpful distinctions are colonic site of involvement, advanced disease and presence of cyclin D1. Correct subclassification of GI lymphoma has important implications for both treatment and prognosis and even small lesions, should be biopsied.[figure1]



## 266

### *Clostridium difficile* Small Bowel Enteritis

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**Purpose:** *Clostridium difficile* infection is usually localized to the mucosa of the large intestine. Isolated *C. difficile* infection of the small bowel mucosa is a rare finding.

**Methods:** A 40 y/o male with past medical history of ulcerative colitis, who underwent a total colectomy with ileostomy in December of 2005 and a take down of ileostomy and re-anastomosis 6 months later, was admitted in July of 2006 with complaints of shortness of breath and diarrhea. Abdominal series showed multiple air fluid levels suspicious for small bowel obstruction. Further work up, which included a computer tomography of the abdomen and small bowel series, showed no evidence of obstruction. During this hospitalization, patient developed an urinary tract infection which was treated with Levofloxacin. Two days after, his diarrhea increased in frequency, at times with blood. *C. difficile* toxin test was positive. Metronidazole was started and the patient improved, eventually leading to discharge. This patient returned in August with hypotension, tachycardia and diarrhea. Repeat CT scan of the abdomen showed diffuse mesenteric fat stranding suggesting mesenteric inflammation. Repeat *C. difficile* toxin test was positive. At that time IV Metronidazole and Vancomycin oral was started. Supportive treatment was given. A flexible sigmoidoscopy was done with findings of erythematous small bowel mucosa, but no pseudomembranes observed. Biopsy results showed small bowel mucosa with preserved villous architecture and no significant pathology. Patient was discharged with oral Vancomycin and appropriate follow up.

**Conclusion:** *Clostridium difficile* small bowel enteritis is rare and only a few cases have been reported. A review of the these cases by the Division of Infectious Diseases at the Wright Patterson Medical Center in 2001 suggested that small bowel enteritis caused by *C. difficile* can be more severe, often leading to death, than the more commonly known colonic mucosa infection. In this case, persistence of the infection despite adequate treatment seems to confirm the aforementioned observations. Our patient developed signs of sepsis and is our belief that this was due to the *C. difficile* infection. Recent reports of ileal perforation secondary to *C. difficile* small bowel enteritis make this infection an important consideration in the differential diagnosis of diarrhea, especially in the setting of colectomy. Therefore, prompt diagnosis and use of adequate therapeutic options seems to be imperative in cases of suspected *C. difficile* small bowel enteritis.

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### Histopathology Predicts Abnormal Liver Function Tests and Autoimmune Disorders in Celiac Disease

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**Purpose:** Celiac disease (CD) is an immune mediated response to gluten characterized by lymphocytic infiltration and/or destruction of intestinal villi. CD has also been associated with extraintestinal manifestations (EIM), unrelated to malabsorption, such as liver dysfunction and autoimmune disease. EIM may result from a breakdown in the gut barrier. We therefore propose that the EIM of CD correlates with more advanced histology.

**Methods:** This was a cross sectional study of 136 patients undergoing endoscopy and duodenal biopsy for upper digestive symptoms or suspected celiac disease. CD was defined as a Marsh III lesion or a Marsh II lesion with positive serologies (PS) for transglutaminase (tTG) and/or antiendomysial antibodies (EMA). 48 patients had Marsh III histology, 14 patients had a Marsh II lesion with PS, while 31 patients had increased intraepithelial lymphocytes (IELs) with negative serologies (NS) and 43 control patients had normal duodenal histology. Presence of elevated liver function tests (LFTs) and serological or clinically documented evidence of autoimmune disorders (AI) at or near the time of diagnosis of CD were recorded. Patients

with abnormal LFTs secondary to an identifiable cause of liver disease were excluded. Statistics was done using SPSS.

**Results:** In patients with Marsh III lesions, 18 (39%) had elevated LFTs and 9 (19%) had AI. In Marsh II patients with PS, 2 (15%) had elevated LFTs, 6 (43%) had AI. In patients with Marsh II lesions alone, 6 (22%) had elevated LFTs, 7 (26%) had AI. Elevated LFTs were seen in 4 (9%) controls and 3 (1%) of these patients had AI. Differences in LFTs between Marsh III lesions and Marsh II lesions with PS and Marsh II lesion without PS and controls were significant (Chi square,  $P = 0.009$ ). Abnormal LFTs were more frequent with advanced Marsh stage. Differences in AI were also significant between the groups (Chi-square  $P = 0.018$ ) but were associated with presence of intraepithelial lymphocytes (IELs) rather than histologic stage. In our population, the odds ratio (OR) of having increased LFTs with celiac disease is 4.26 (CI 95% = 1.15–15.76). The OR of having AI with IELs is 3.08 (CI 95% 1.30–7.27).

**Conclusion:** In CD, higher Marsh levels are associated with an increased frequency of abnormal LFTs. Though no such association is seen with autoimmunity there appears to be an increased incidence of AI with the presence of increased IELs.

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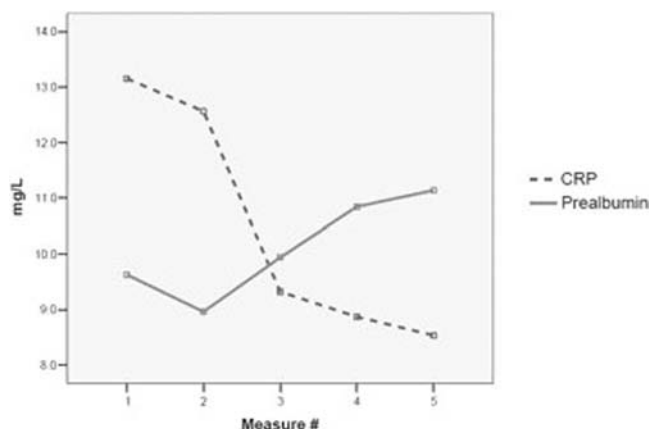
### Is Pre-Albumin an Accurate Marker of Nutritional Status in Acutely Ill Patients?

Kandarp R. Patel, DO, Lin Shu, Richard Gerkin, MD, Rakesh Nanda, MD\*. Department of Gastroenterology, Carl T. Hayden VA Medical Center, Phoenix, AZ and Department of Medicine, Good Samaritan Regional Medical Center, Phoenix, AZ.

**Purpose:** Pre-Albumin (PAB), a hepatic protein, is the earliest laboratory indicator of nutritional status and is the preferred marker for “malnutrition” as it correlates with patient outcomes in a wide variety of clinical conditions. PAB is also a negative acute phase protein whose plasma concentration decreases during inflammation. The aim of this study was to determine if PAB is a valid indicator of the nutritional status in patients with acute inflammation.

**Methods:** We retrospectively reviewed all admissions over a 2 year period from 1/1/2004 to 12/1/2005. Patients included in this study were inpatients who had PAB and C Reactive Protein (CRP) drawn on the same day. Admissions to all services, including medical, surgical, and ICU were included in the analysis. Analysis was performed using SPSS software and the extent of the relationship was found by calculating the Spearman  $\rho$  correlation coefficient. A  $P$ -value less than .05 was considered significant.

**Results:** 176 patients were analyzed. Multiple values were collected on single patients for a total of 316 specimens. The Spearman  $\rho$  correlation coefficient on day 1 was  $-.625$  ( $P < .001$ ), day 2 was  $-.513$  ( $P < .001$ ), day 3 was  $-.791$  ( $P < .001$ ), day 4 was  $-.770$  ( $P < .001$ ), and day 5 was  $-.742$  ( $P < .004$ ). [figure1] All results showed a statistically significant negative



correlation between CRP and PAB levels. As the figure also shows PAB levels increased only when CRP normalized.

**Conclusion:** Currently there is no single reliable indicator of patients' nutritional status and by default PAB is the most widely used because of its ease to perform. Our study did show there is a negative correlation between acute inflammation and PAB. Also, as CRP levels normalized the PAB levels increased. Our study suggests PAB may not be an accurate marker of assessing nutritional needs in acutely ill patients. Future prospective controlled studies will be needed to confirm our hypothesis.

## LIVER

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### Problems in Determining the Etiology for High “No-Show” Rate of Patients Referred for Evaluation of Hepatitis C

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**Purpose:** In a recent prospective study, it has been substantiated that patients referred for evaluation of hepatitis C are less likely to show for their initial outpatient consultation, than those referred for the evaluation of “all other” gastroenterologic/hepatologic diagnoses. This investigation sought to determine the etiology for this phenomenon.

**Methods:** In a previously performed prospective study, it was shown that patients referred to a gastroenterologist (private-practice, single-specialty gastroenterology group in a semi-rural community), were less likely to “show” for their initial office consultation if referred for evaluation of hepatitis C, than if they had been referred for “all other” gastroenterologic/hepatologic diagnoses. Over the study period (10/3/03 through 5/6/05), 543 new patients were scheduled for initial outpatient office consultation. Of these, 66 were referred for evaluation of hepatitis C, and 477 were referred for evaluation of “all other” diagnoses. The rate of “not-showing” for initial consultation was 12/66 = 18.2% for patients presenting for evaluation of hepatitis C versus 37/477 = 7.8% for patients referred for evaluation of “all other” diagnoses, ( $P = 0.01$  by Fischers exact test; odds ratio = 2.65).

From 5/7/05 through 3/21/07 a total of 6 patients referred for evaluation of hepatitis C did not “show” for initial consultation. A brief questionnaire (with enclosed self-addressed/stamped return envelope) was sent to these patients in an attempt to elucidate the reason for this phenomenon.

**Results:** Of the 6 questionnaires which were mailed to these patients, none were returned.

**Conclusion:** The reason why patients with hepatitis C often fail “to show” for initial outpatient office consultation remains unclear. This uncertainty remains, despite attempting to contact a cohort of such patients by mail (with a brief questionnaire and enclosed self-addressed/stamped return envelope). This “failure to show” for initial subspecialty consultation is clearly one major impediment in the pathway to the adequate evaluation and treatment of patients with hepatitis C.

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### Hepatic Neuro-Endocrine Tumor: A Case Report

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**Purpose:** Primary hepatic neuroendocrine tumor are underreported in literature as they are thought to represent metastatic lesions. We present a rare case masquerading as HCC accompanied by high AFP secretion.

**Methods:** The patient presented with a history of weight loss and abdominal pain that began in right upper quadrant. Lab work showed: Hgb 12.6 gm/dl, calcium 10.5 mg/dl, creatinine 1.8 mg/dl, lipase 561 U/L, AST 151 IU/L, ALT 51 IU/L, T bil 1.2 mg/dl, Alk. phos 262 IU/L, AFP 10313 ng/ml and a

CEA level of 4.3 ng/ml. Hepatitis panel was non reactive. CT scan showed enlarged liver with multiple large areas of diminished attenuation consistent with multiple hepatic masses. An FNAC of liver showed the cell block to be entirely composed of necrotic tumor with groups of tumor cells demonstrating high nuclear to cytoplasmic ratio, numerous mitotic figures, granular chromatin, no visible nucleoli and a vague rosette-like pattern. Percutaneous liver biopsy specimens were initially reported as hepatocellular carcinoma but were later revised to neuroendocrine tumor on immunohistochemical review. A core biopsy was done to further characterize the histology, which was consistent with neuroendocrine tumor. On immunohistochemistry, the tumor cells were positive for chromogranin and synaptophysin and negative for cytokeratin 7 and 20. His serum chromogranin A level was 839.5. Extensive work up failed to yield a primary site of neuroendocrine tumor involvement. He was thus diagnosed with an atypical neuroendocrine tumor and palliative chemotherapy with carboplatin and etoposide treatment was initiated.

**Results:** Although an AFP level of >500 is considered diagnostic of Hepatocellular carcinoma, liver biopsy with immunostaining techniques is necessary for proper diagnosis and treatment in cases where a neuroendocrine involvement is suspected. An apparent hepatic carcinoid tumor may be metastatic disease, where despite extensive assessment the primary tumor remains obscure. Most primary hepatic neuroendocrine tumors are endocrinologically silent. The mainstay of treatment is hepatic resection while octreotide is best suited for metastatic disease from a primary hepatic neuroendocrine tumor. Regular clinical review and CT imaging are essential to detect recurrence. The overall prognosis with this tumor is better than for other hepatic carcinomas.

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#### Liver Transplantation and Neurological Manifestations in Wilson Disease

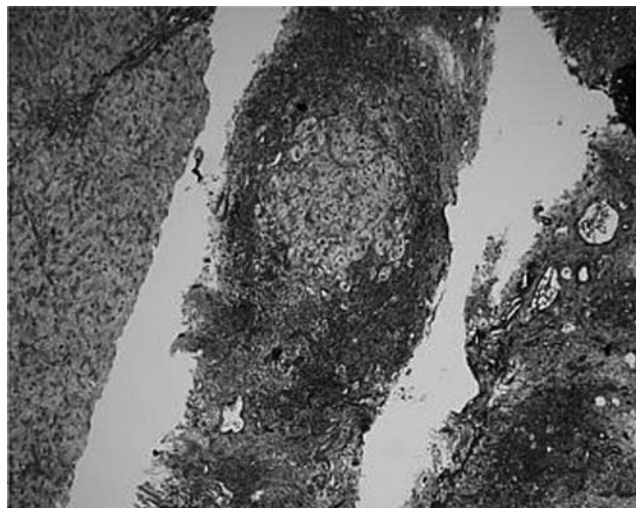
Sumit Sharma, MD, Preeti Agrawal, MD, Shan-Ching Ying, MD, Kris Ananad, MD, Arun Verma, MD\*. Medicine, Rosalind Franklin University of Medicine and Science, North Chicago, IL and Pathology, Mt. Sinai Hospital, Sinai Health System, Chicago, IL.

**Purpose:** The role of liver transplantation (LT) in managing the neurological manifestations of Wilson's Disease (WD) is not yet conclusive. A 26 year-old man with WD with cirrhosis experienced a dramatic improvement in motor function and cognitive testing early after LT, as well as normalization of copper balance.

**Methods:** A 26 y/o Hispanic man presented with progressively increasing abdominal distension, dark urine, clumsiness of gait and cognitive deficits. He did not have any history of emotional disorder/drug or alcohol dependence/suicidal ideation/hallucinations. On physical examination he had a tense, distended abdomen with diffuse tenderness, BS+, liver and spleen could not be palpated. Imaging revealed a large ascites and splenomegaly ( $9.5 \times 18 \times 19$  cm) without parenchymal lesions. Liver had a nodular contour and coarse echo pattern. CT of the Abdomen/Pelvis revealed massive ascites with a small, shrunken, irregular liver with nodular periphery. Patient was started on lasix, spironolactone and lactulose. EGD showed portal gastropathy and Grade 1 esophageal varices and ophthalmologic evaluation did not show KF rings. Laboratory studies showed Iron Deficiency anemia with normal antibody levels of ANA, AMA, alpha 1 antitrypsin and anti Sm Ab. SAAG > 1.1 with 24 Hr urinary copper level of 1835 mcg/l and ceruloplasmin level of 3 mg/dl, liver copper 974 mcg/gm (dry wt) was consistent with Wilson's disease. Patient was started on D-Penicillamine and subsequently put on trientine due to heavy proteinuria and referred for a liver transplant. He finally got a liver transplant (sibling) and currently is in good health without any neurological deficits and marked cognitive improvement.

**Results:** Asonuma *et al* reported that LRLT from heterozygous carriers of the WD gene could resolve clinical signs and symptoms of WD and correct the parameters of copper metabolism. In this case study, Copper metabolism in the WD recipient was compared before and after transplantation with

marked reduction in urinary copper excretion. Long-term follow-up should be continued to evaluate this specific therapy.[figure1]



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#### Etiological, Clinical and Radiological Profile of Suppurative Lesions in Solid Abdominal Visceras

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**Purpose:** The profile of abscess is changing over last few decades in the developing world. A few decades earlier the liver abscess in our country was invariably amoebic in nature, however, in recent times the pyogenic and mycotic abscess are being recorded with increasing frequency. This study aims to evaluate the etiological, clinical and radiological profile of suppurative lesions in intraperitoneal solid visceral organ like liver and spleen in our tertiary health care centre in North India.

**Methods:** A total of 35 patients with intrabdominal abscess were prospectively evaluated over a period of one year in the Department of Gastroenterology, IMS, BHU, Varanasi (India). They were studied to detail clinical, hematological, biochemical, microbiological and radiological examination. Few special investigations like HIV testing, blood culture and ELISA for *E. histolytica* antibody were also carried out in our study.

**Results:** Of the 35 cases, 30 had liver abscess and 5 splenic abscesses. There were significant changing trend on the incidence of amoebic abscess (70%) and pyogenic abscess (30%). Majority of patients with amoebic abscess presented a decade earlier than pyogenic abscess group. Anemia, moderate polymorphonuclear leukocytosis, elevated serum bilirubin, increased serum alkaline phosphatase, increased SGOT, increased SGPT, hypoalbuminemia were significantly observed in our study group. Most frequently isolated organism was *Klebsiella pneumonia* (10%) followed by *E. coli* (6.6%) and *Staph aureus* (3.3%). Amoebic abscess were mostly solitary (size > 7 cm), echofree wall and subcapsular. Males were the dominant group in both liver and splenic abscess.

**Conclusion:** Profile of suppurative disease affecting solid abdominal viscera is changing. Two decades earlier it was invariably involved liver of amoebic nature. In this study two fifth of cases were due to pyogenic abscess in which gram negative organism were predominantly isolated, affecting liver (26%) and spleen (14%), HIV coinfection was an important accompaniant (40%) in splenic abscess and chronic alcohol is seen in amoebic liver abscess (76.1%).

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#### Transjugular Intrahepatic Portosystemic Shunt (TIPS) in Budd-Chiari Syndrome (BCS): Experience at a Tertiary Health Center



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**Purpose:** Transjugular intrahepatic portosystemic shunt (TIPS) is a technically challenging but efficient therapeutic tool in patients with Budd-Chiari syndrome (BCS). Results from several small series appear promising but long-term outcome is not well studied. We aimed to analyze the results of TIPS as a treatment option in BCS and compare the outcome of PTFE-covered stents vs bare stents.

**Methods:** Of 148 patients of Budd-Chiari syndrome, 115 underwent vascular interventions. 17 patients underwent TIPS/ modified TIPS. Patients were followed 3–6 monthly with clinical and biochemical assessment, color doppler and; venography yearly.

**Results:** 17/18 (94.4%, male-12, median age  $30 \pm 11.7$ ) patients underwent successful procedure. Median duration of symptoms to diagnosis was 3 months. Presentation was acute, subacute and chronic in 4, 6 and 7 cases, respectively. Indications were ascites (15/17) and variceal bleed (2/17) which were controlled in all. Ten and 7 received PTFE covered and bare stents respectively. In addition to hepatic vein occlusion, 3 had IVC block for which IVC stenting was done. Total follow up period was 21 months (range 1–52 m). Five stent dysfunctions and repeat interventions were required in 4 patients with uncovered stents (median 22 months range 2–55 months) vs 2/10 with PTFE-covered stents (median 18 months range 1–34 m) ( $P = 0.0339$ ). One year actuarial primary patency rates were 80% vs 57.5% in PTFE-covered stent group vs uncovered stent group. There were 2 deaths; 1 patient developed intraperitoneal bleed and died 30 days later and the other patient died 4 months later because of variceal bleed and complications precipitated by TIPS dysfunction.

**Conclusion:** TIPS is a useful modality of treatment for BCS with nonre-canализable hepatic veins. PTFE Covered stents may be better than uncovered stents.

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### The Effect of Statins on PEG-Interferon/Ribavirin Treatment for Chronic Hepatitis C

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**Purpose:** There is evidence that HMG-CoA reductase inhibitors (statins) have an effect on hepatitis C virus (HCV) replication *in vitro*. We hypothesize there is a synergistic effect of statins when combined with interferon-based treatment. We conducted a retrospective review to evaluate the effect of statins on PEG-interferon (PEG-IFN) plus ribavirin (Rib) treatment response in treatment-naïve patients (pts).

**Methods:** We identified all pts seen from 2001–06 who had chronic HCV, were naïve to treatment with IFN-based therapy, and were taking a statin during their course of PEG-IFN/Rib therapy ( $N = 13$ ). The study group was matched in 1:3 fashion to 39 control pts for gender, ethnicity, genotype, and presence of cirrhosis, and we compared these groups for response to first time treatment with PEG-IFN/Rib. We excluded pts with active HIV/HBV infection or had received previous IFN-based therapy. We collected data on age, BMI, and HCV viral load (VL). VLs were recorded at baseline, 12 wks after start of treatment, end of treatment, and 24 wks after completion of treatment.

**Results:** In our study, pts were male (100%) of caucasian ethnicity (76.9%) with genotype 1 (61.5%) and cirrhosis in 7.7%. Statin group pts had mean age 51.1 yrs with BMI 30.6 with mean baseline  $\log_{10}$  VL 5.98 and were comparable to control pts. In the study group, EVR (2 log decrease in VL @ 12 wk) was achieved in 100% pts, ETR in 76.9% pts, and SVR in 38.5% pts. In the control group, EVR was achieved in 86.8% pts, ETR in 52.6% pts, and SVR in 34.2% pts. There was no statistical difference measured between proportions of statin pts and control pts achieving EVR, ETR or SVR. However, the statin group had a higher proportion of undetectable VL

(91.7% vs 55.6%,  $P = .02$ ) and lower mean  $\log_{10}$  VL (.4 vs 1.7,  $P = .04$ ) at 12 wks after start of treatment. 11 statin pts (84.6%) and 29 control pts (74.3%) completed the full treatment course.

**Conclusion:** While there was no difference in proportions between the statin vs control pts for achieving EVR, ETR, or SVR, there was significantly higher proportion of statin pts with undetectable HCV VL at 12 wks of treatment. It is possible that there is a significant synergistic effect of statins with IFN-based therapy. Higher proportion of complete EVR with statins may ultimately have significant impact on SVR; however, larger, prospective trials are needed.

	Results		
	Statin Pts	Control Pts	P
% EVR	100%	86.8%	NS
% Complete EVR	91.7%	55.6%	.02
% ETR	76.9%	52.6%	NS
% SVR	38.5%	34.2%	NS

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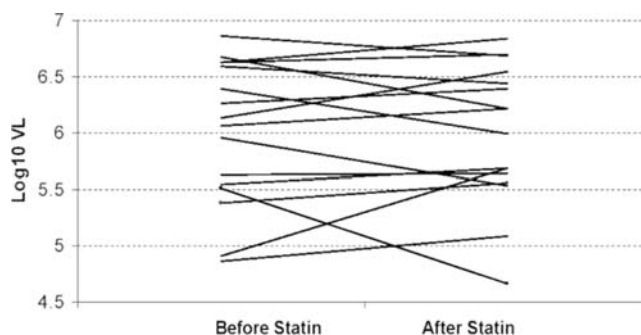
### The Effect of Statins on Viral Load in Patients with Chronic Hepatitis C

Roy D. Yen, MD, Anoop Prabhu, MD, Thomas Mahl, MD\*. Internal Medicine/Gastroenterology, VA Western New York Healthcare System, Buffalo, NY.

**Purpose:** There is some evidence that HMG-CoA reductase inhibitors (statins) have an effect on hepatitis C virus (HCV) replication *in vitro*, but there is no *in vivo* data. We conducted a retrospective review from one large healthcare network database to evaluate the effect of statins on viral loads (VLs) in patients chronically infected with HCV.

**Methods:** We identified all patients seen between 2000–06 who had chronic HCV, were prescribed a statin, and had HCV VLs measured before and after the initiation of statins ( $N = 16$ ). We excluded patients with chronic hepatitis B or HIV infection or those receiving active treatment for HCV. We collected data on age, gender, ethnicity, BMI, self-reported alcohol use, specific statin medication and dose, HCV serology and genotype, LFTs and lipid profile. We compared the change in HCV VLs before and after initiation of statins by Wilcoxon Signed Rank test. All significant  $P$  values reported for  $P < .05$ .

**Results:** In our study, patients were males (100%) of Caucasian ethnicity (80%) with mean age 55.5 yrs and BMI 29.7. The median  $\log_{10}$  VL prior to initiation of statin was 6.094. Most patients had genotype 1 (80%). Majority of patients were prescribed simvastatin (87.5%) with mean dose of 35.4 mg. Patients were taking statins for mean 430.4 days prior to having HCV VL rechecked with median  $\log_{10}$  VL 6.103 at that time. There was no significant difference between HCV VL before and after initiation of statin ( $P = .96$ ), and there was also no significant change in LFTs after statins were started.



However, there was a significant decrease in total cholesterol after statins were started ( $P < .001$ ).

**Conclusion:** Our review did not demonstrate a significant change in HCV levels after initiation of statin. However, larger, prospective studies are required.[figure1]

	Results		<i>P</i>
	Before Statin	After Statin	
Log <sub>10</sub> VL	6.094	6.103	.96
AST	42	49	.33
ALT	64	79	.69
Total Chol	200	149.5	.001

Median values reported

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### Results of 5 Years Experience of Liver Secondaries Treated by Radiofrequency Ablation

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**Purpose:** Radiofrequency ablation (RFA) is a new percutaneous tissue ablative therapy. Role of RFA in treating liver secondaries is not widely studied. We present our 5 years experience of RFA of liver secondaries.

**Methods:** Using Berchtold (Tuttlingan, Germany) RF generator (50–60 watt output), 1500–2000 watts energy/cc tumour was delivered according to the volume of liver secondaries.

Inclusion criterias were: lesion <5 cm in size, Non-invasion of portal vein, no proximity to large vessel or duct technically feasible.

Exclusion criterias were: extra-hepatic disease not being treated by chemotherapy, diminished hepatic function (eg. Child Pugh Class C), refractory coagulopathy, massive ascites.

Between February 2001 and October 2006, 81 patients (52 males and 29 females), aged 39 to 72 years (mean 56 years) had RFA of 252 liver secondaries from gall bladder = 22, colorectal = 36, breast = 14, carcinoid or neuroendocrine = 5, stomach = 4 cancers.

Lesions were sized <3 cm in 69, 3–4 cm in 118 and >4 cm in 65.

RF needle was placed, US guided in 76, CT guided in 1 and at an open surgery in 4 patients. Follow up was done by contrast enhanced CT scan between 1–4 weeks after the procedure.

**Results:** There was no procedure related mortality. All patients were discharged within 24 hours except two. There was no major morbidity. There were 10/81 (8%) minor morbidity (self limiting ascites = 3, severe abdominal pain = 3, self limiting pleural effusion = 4). *Efficacy:* Complete necrosis was seen in all (100%, 69/69) of lesion up to 3 cm size and (40.6%, 48/118) of lesion 3–4 cm in size. None of the lesion >4 cm had complete necrosis. Recurrence at completely treated site at mean follow up of 12 months was 10/117 (8.54%). On more than 12 months follow up, 51/81 (63%) patients developed new hepatic or systemic recurrence. *Survival:* One year survival was 59% and 2 year survival was 24% of whole group.

**Conclusion:** RFA is safe and effective local tissue ablative method for liver secondaries. More randomized trials are required to ascertain efficacy of RFA in improving quality of life and /or survival in patients with liver secondaries.

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### A Single Center Experience of the Use of Mycophenolate Mofetil (MMF) in the Maintenance Treatment of Autoimmune Hepatitis (AIH)

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**Purpose:** AIH is a common disease in women which has traditionally been treated with prednisone (P) ± azathioprine (AZA). However, some patients (pts) are intolerant or do not respond to AZA. MMF, like AZA, is an antimetabolite with a somewhat less toxic side effect profile. The objective of this study was to assess the clinical utility of MMF in the maintenance treatment (tx) of AIH.

**Methods:** We performed a retrospective longitudinal analysis of pts followed by Hepatology at VCUHS with AIH diagnosed by liver histology and autoantibodies (ANA and ASMA). Pts with viral hepatitis, overlap syndrome and other liver diseases were excluded. Demographic and clinical data at presentation were collected. Baseline characteristics and effectiveness of maintaining remission were compared between those who received to standard therapy (P ± AZA) and those who received MMF.

**Results:** We identified 126 pts with AIH: mean age 43, 84% female, 69% Caucasian, 61% + ANA, 48% + ASMA. At presentation, median AST and ALT were 227 and 261 while bridging fibrosis or cirrhosis were present in 38% and 22%, respectively. After initial induction, maintenance tx included P + AZA (N = 85), P + MMF (N = 16), low dose P (N = 7), AZA (N = 7), MMF or tacrolimus (1 each). Of the 88 who initially received P ± AZA, 12 were switched to MMF (main reasons for conversion: nausea/vomiting (N = 4), failure to normalize LFTs (N = 3), and pancreatitis, DVT, rash, intolerance or hair loss (1 each). Of the 28 on MMF, 10 eventually discontinued MMF due to side effects: headache (N = 3), failure to normalize LFTs (N = 3), nausea/vomiting (N = 3), and myalgias (N = 1), while 18 remained on MMF either alone (N = 4) or combined with P (N = 12) or P + tacrolimus (N = 2). Of the 28 on MMF at any time, remission rates were similar (86%) to those who remained on standard therapy P ± AZA (81%). The only independent factor that predicted the eventual need for conversion to MMF was cirrhosis at presentation ( $P = .0036$ ).

**Conclusion:** 1) Use of MMF in the treatment of AIH was well tolerated; 2) Cirrhosis on presentation was the only independent factor associated with eventual need for MMF; and 3) Use of MMF was associated with a high rate of remission (86%). Therefore, we conclude that MMF is an effective option for salvage therapy for AIH in those who can not tolerate or fail to respond to AZA.

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### The Risk of Analgesics in Cirrhotics

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**Purpose:** Analgesics, including nonsteroidal anti-inflammatory, acetaminophen and aspirin containing compounds may lead to complications of cirrhosis through a variety of mechanisms. The aim of this case control study was to assess the association between analgesic use and hepatic decompensation leading to hospitalization in patients with cirrhosis.

**Methods:** We prospectively enrolled 90 non-encephalopathic cirrhotic cases admitted with acute decompensation events, comprising portal hypertensive bleeding, ascites, peritonitis, and 125 non-hospitalized cirrhotic controls. We ascertained 30-day analgesic use and potential confounding factors for hepatic decompensation such as non-analgesic and alternative medication use, alcohol use and dietary/medication compliance. All controls had a history of decompensation, indicating that cases and controls were roughly at similar risk for decompensation due to cirrhosis alone. Cognitive function was assessed using the Mini Mental State Examination. Univariate and multivariate logistic regression were used for the analyses. Unadjusted and adjusted odds ratios were computed, along with corresponding 95% confidence intervals and *P*-values.

**Results:** Hepatitis C, alcohol, and cryptogenic cirrhosis, were the most common etiologies of cirrhosis, in 168 (79%) of the study patients. The distribution of etiologies was not significantly different between cases and controls. Overall, 34% of cases and 44% of controls reported analgesic use over the

30 days prior to the interview however the difference was not statistically significant. Multivariate logistic regression indicated that, after controlling for confounding factors analgesic use was not significantly associated with decompensation (adjusted OR = 0.69,  $P = 0.234$ ). These patterns were consistent for all classes of analgesics (nonsteroidals and acetaminophen containing). However, there was a trend toward decompensation (adjusted OR = 2.02) among those who took analgesics 4 weeks prior, although that effect was not statistically significant ( $P = 0.112$ ).

**Conclusion:** Our results suggest that analgesics do not put cirrhotics at increased risk for decompensation. The lack of an expected deleterious effect of analgesics may be explained by infrequent use and low doses. However, the trend toward higher risk for decompensation among those who used analgesics four weeks prior indicates that an effect may exist and warrants further investigation.

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### Role of Vitamin E & Vitamin C in the Treatment of Nonalcoholic Steatohepatitis

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**Purpose:** To determine whether supplemental vitamin E & C lowers serum aminotransferases in patients with nonalcoholic steatohepatitis.

**Methods:** We did a retrospective analysis of NASH patients who were seen in the AGH Centre for Digestive Health. We evaluated patients age 18 and 75 years with biopsy proven NASH and exclusion of other chronic liver diseases. A total of 68 patients who met study criteria were assessed retrospectively & baseline characteristics including age, sex, weight, BMI, HTN, DM, lipid profile, AST, ALT, ALP were collected. 68 patients were divided in two groups: supplemental vitamin E & C ( $N = 38$ ) or no vitamin supplements (control group) ( $N = 30$ ). Doses of vitamin E & C were 400 IU–800 IU and 500 mg–1000 mg respectively. AST, ALT, ALP and weight data were collected between 2–24 months from baseline. The mean follow up period was 11.96 months and 11.37 months for vitamin group and non vitamin group respectively. Baseline and follow up data were compared using the paired t test or Wilcoxon signed rank test. Differences between the groups were compared by independent sample t test or the Mann-Whitney rank sum test.

**Results:** Baseline characteristics were similar in the Control and Vitamin C & E groups. Weight, ALT and ALP were similar in Control subjects between baseline and follow up; mean AST was higher at follow up. Mean ALT was 99.6 U/L at baseline and significantly decreased to 63.7 U/L ( $P < 0.001$ ) after vitamin C & E use. Mean AST was 68.5 U/L at baseline and significantly decreased to 41.2 U/L after vitamin C and E use ( $P < 0.001$ ). Mean ALP was 101.3 U/L at baseline and decreased to 83.8 U/L at follow-up ( $P = 0.09$ ). Mean weight was comparable between baseline and after use of vitamins C & E (210.8 lb  $\pm$  36.6 vs. 210.8 lb  $\pm$  36.0,  $P = 1.0$ ). Changes from baseline in mean ALT, AST and ALP were greater in subjects who took vitamins C & E than in Controls; these differences were statistically significant. Mean ALT decreased from baseline -35.9 in the Vitamin C & E group and increased from baseline +9.9 in the Control group ( $P < 0.001$ ). Mean AST decreased from baseline -27.3 in the Vitamin C & E group and increased from baseline +11.2 in the Control group ( $P < 0.001$ ). Mean ALP decreased from baseline -16.6 in the Vitamin C & E group and increased from baseline +4.2 in the Control group ( $P = 0.049$ ).

**Conclusion:** Vitamin E & C is effective in lowering serum aminotransferases in patient with nonalcoholic steatohepatitis. Our study showed improvement in serum aminotransferases within group and between groups.

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### To Investigate the Utility of a Week-4 Virological Response for SVR Prediction in Hepatitis C Virus (HCV) Genotype 3 Patients Treated with Pegylated Interferon and Ribavirin for 24 Weeks

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**Purpose:** To investigate the utility of a week-4 virological response for SVR prediction in hepatitis C virus (HCV) genotype 3 patients treated with Pegylated interferon and ribavirin for 24 weeks.

**Methods:** Using a PCR-based quantitative assay we analysed samples obtained at baseline and weeks 4 and 12 from a subset of 50 HCV genotype 3 patients enrolled in a randomized trial of peginterferon a-2a in combination with ribavirin.

**Results:** In an intention-to-treat analysis, 84% of patients treated with peginterferon achieved a sustained virological response (SVR). At 4 weeks, 50% of patients had HCV RNA  $< 50$  IU/ml and 65% had  $< 600$  IU/ml. Of these rapid responders 86 and 87% achieved a SVR, respectively, with 2 patients relapsing. In contrast, only 44 and 31% of patients with a week-4 HCV RNA  $< 50$  or  $< 600$  IU/ml achieved an SVR, respectively, with relapse rates of 23 and 55%, respectively. In multivariate logistic regression analysis a serum HCV RNA level below 600 IU/ml at week 4 was the strongest independent predictor of SVR (odds ratio, 11.5; 95% confidence interval, 1.5 to 65.0;  $P = 0.015$ ).

**Conclusion:** Monitoring early viral response may be useful to tailor the duration of treatment among patients with HCV genotype 3. Patients whose HCV RNA falls below 600 IU/ml at 4 weeks are at low risk of relapse after 24 weeks of combination therapy.

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### Hepatitis B (HBV) Patients Undergoing Chemotherapy: Who Gets Screened and What Prophylaxis Is Given? A Questionnaire Survey of Oncologists

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**Purpose:** Chemotherapy is well-described as a risk factor for reactivation of HBV infection, although the degree of awareness of this potentially fatal complication has not been well studied among practicing oncologists.

**Methods:** We developed a questionnaire that was verbally administered to 131 Heme-Onc physicians in the Washington, DC metropolitan area in early 2007 that sought to assess their awareness of Hep B reactivation, their current practice of screening for HBV and their recommendations for giving antiviral prophylaxis to their chemotherapy patients.

**Results:** Respondent answers as follows: (1) Are you aware that reactivation of HBV can occur with chemotherapy? Yes 78%; No 22%. (2) Have you ever seen HBV reactivation in this setting? Yes 30%; No 70%. (3) Which patients do you screen for HBV: abnormal LFTs 70%; from Asia or Africa 32%; coinfectd with HCV 70%; coinfectd with HIV or Hx IDVU 58%; healthcare worker 50%; Hx of transfusions 54%; homosexual men 60%. (4) Which HBV pt should receive prophylaxis? chronic carrier 46%; active infection 76%; resolved HBV 52%. (5) Do you prescribe prophylaxis yourself? Yes 28%; No 72%. (6) Which antiviral therapy would you use? Lamivudine 46%; adefovir 14%; not sure 48%. (7) How would you monitor for HBV reactivation? LFTs 46%; viral serology 36%; clinical signs/Sxs 32%; not sure 26%. (8) How frequently would you monitor? q2 wk 4%; q4 wk 18%; q6 wk 14%; q8 wk 16%; q12 wk 12%; not sure 36%. (9) How long should prophylaxis continue after chemotherapy? 4 wk 8%; 8 wk 15%; 12 wk 71%; 16wk 8%. (10) Would you want a gastroenterologist/hepatology to follow the pt during prophylaxis? Yes 88%, No 12%; and after prophylaxis? Yes 26%, No 74%.

**Conclusion:** Most practicing oncologists have not personally encountered HBV reactivation during chemotherapy, and relatively few currently screen universally for HBV or are aware that antiviral prophylaxis is available. Over 80% would defer treatment to a specialist. Raising awareness among oncologists of current recommendations for screening and providing HBV prophylaxis to chemotherapy patients is clearly warranted.

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### Leucocyte Esterase Reagent Strips for the Diagnosis of Spontaneous Bacterial Peritonitis: A Systematic Review

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**Purpose:** Spontaneous bacterial peritonitis (SBP) is a potentially life-threatening complication of decompensated liver disease. Ascitic fluid polymorphonuclear (PMN) count  $\geq 250/\text{mm}^3$  objectively confirms SBP. The existing "gold standard" for the evaluation of ascitic PMN count (manual count) is however laborious and time-consuming. Recently leukocyte esterase reagent (LER) strips (common urine dipsticks) have been successfully used for the diagnosis of infection in various body fluids. The test is based on the esterase activity of PMN. Hence, they provide a cheap, easily accessible and rapid method for the diagnosis of PMN presence in the ascitic fluid.

**Aims:** We aimed to systematically review the existing evidence on the diagnostic value of LER strips in SBP.

**Methods:** Comprehensive literature search of Medline up to April 2007 for human clinical trials comparing LER strips with manual count of PMN in ascitic fluid. MeSH terms used included ["ascites" OR "ascitic fluid" OR "peritonitis"] AND ["reagent strips" OR "Leuc(k)ocyte esterase strips"]. Abstracts reviewed independently by two authors and full papers of relevant studies were obtained.

**Results:** We identified 16 relevant studies (thirteen in English and from 1 in French, Chinese and Korean) comprising 2519 patients. Thirty of them were Child-Pugh (CP) stage A, 849 CP-stage B, and 1267 CP-stage C. A total of 4730 paracenteses was performed. A total of 521 SBP was diagnosed. Various dipsticks were evaluated; Nephur (2 times), Multistix 10SG (7 times), Aution (1 time), UriScan (2 times), Multistix 8SG (5 times) and Combur tests (5 times).

Compared to manual count of PMN ("gold standard"), LER strips were found to have sensitivity ranging from 45.3% to 100%; specificity ranging from 84.75% to 100%; positive predictive value ranging from 42% to 100%; negative predictive value ranging from 87% to 100%.

**Conclusion:** Use of LER strips in ascitic fluid is a useful method for the early diagnosis of SBP.

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### Splanchnic Hemodynamics in Cirrhotic Patients: Relationship to Esophageal Varices and the Severity of Hepatic Failure

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**Purpose:** The relationship between splanchnic hemodynamics, liver function, and esophageal variceal grading in cirrhosis remains unclear. **The aim** was to determine the value of quantitative Doppler parameters of splanchnic hemodynamics in assessing esophageal variceal (OV) grading, severity of liver insufficiency and presence of ascites.

**Methods:** The following parameters were performed for 153 cirrhotics and 30 controls: portal vein (PV) and splenic vein (SV) – cross sectional area (CSA), mean velocity (MV), flow volume (FL), PV congestive index; hepatic artery, splenic artery (SA) and superior mesenteric artery (SMA) pulsatility index (PI) and resistive index (RI); liver vascular index (LVI), modified LVI (M-LVI), portal hypertension index (PHI), portal inflow (P-flow) and collateral inflow (C-flow).

**Results:** All parameters differentiated between control and cirrhotics except PV-FL and SV-FL which were significantly lower only in advanced cirrhosis

(Child C). SMA-PI, PHI, P-flow and C-flow were significantly different among various Child classes. PV-MV was significantly lower in small OV compared to other groups. All parameters were significantly different in large OV except PV-FL, SMA-PI and -RI. PV-FL, SA-PI, SMA-RI, LVI, M-LVI, P-flow and C-flow were significantly different in gastric varices group compared to other groups. All parameters were significantly different in ascitic than non-ascitic except PV-CSA, SMA-PI and -RI.

**Conclusion:** Splanchnic Doppler parameters are significantly related to stages of liver damage, grade of portal hypertension and presence of ascites, and may therefore be used as surrogate markers. We recommend an optimal scoring system with Doppler parameters integrated for diagnosis and staging of cirrhosis and portal hypertension.

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### Study of Serum Adiponectin in Chronic Liver Disease and Cholestasis

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**Purpose:** Adiponectin is suggested to have a hepatoprotective effect. To date, there is minimal information available in the literature regarding changes in serum adiponectin levels in cirrhosis and cholestasis and the associated metabolic disturbances. Therefore, our *aim* was to elucidate the role of adiponectin in chronic liver disease and to correlate adiponectin level with liver functions & markers of the metabolic syndrome as body mass index and insulin resistance in these patients.

**Methods:** 40 patients with different grades of cirrhosis, 30 patients with cirrhosis & cholestasis and 20 matched controls were studied. They were subjected to clinical assessment, BMI and Child score calculations, analysis of ALT, AST, alkaline phosphatase, GGT, C-reactive protein, HOMA index, adiponectin, abdominal ultrasonography & upper GI endoscopy.

**Results:** Adiponectin was significantly higher in patients than controls (cirrhosis:  $15.1 \pm 12.14 \mu\text{g/ml}$  vs  $4.7 \pm 4.48 \mu\text{g/ml}$ ,  $P < 0.05$  and cirrhosis/cholestasis:  $21.28 \pm 10.2 \mu\text{g/ml}$  vs  $4.7 \pm 4.48 \mu\text{g/ml}$ ,  $P = 0.001$ ). Adiponectin correlated with bilirubin ( $r = 0.369$ ,  $P < 0.05$ ), ALT ( $r = 0.283$ ,  $P < 0.05$ ), AST ( $r = 0.367$ ,  $P < 0.05$ ), albumin ( $r = -0.287$ ,  $P < 0.05$ ), prothrombin ( $r = 0.278$ ,  $P = 0.053$ ), ALP ( $r = 0.394$ ,  $P < 0.005$ ), GGT ( $r = 0.298$ ,  $P < 0.05$ ), CRP ( $r = 0.406$ ,  $P < 0.05$ ). Adiponectin did not correlate with presence of ascites or esophageal varices nor did it correlate with BMI or HOMA index.

**Conclusion:** adiponectin is elevated in cirrhosis and correlates with degree of hepatocellular injury and cholestasis. It could serve as a novel marker indicating cholestasis in liver cirrhosis. Adiponectin in cirrhosis does not correlate with parameters of body composition or metabolism but exclusively with reduced liver function.

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### Independent Predictors of Histologic Disease Severity in Asian Indian Patients with Nonalcoholic Steatohepatitis

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**Purpose:** The clinical and histological spectrum of non-alcoholic steatohepatitis (NASH) is not clearly defined for different races and geographical areas of the world. **Aim:** To study the histologic spectrum and to identify the clinical and biochemical predictors of histologic disease severity in patients with NASH in Asian Indian Population

**Methods:** Seventy-one consecutive patients of NASH were included in the study. Clinical and laboratory data was recorded. Patients were categorized into five BMI based subgroups using Asian criteria. For diagnosis of NASH on liver histology, criteria given by Matteoni et al and at the AASLD

conference (2003) were followed. Histologic features, global necroinflammatory grade and fibrosis stage of liver biopsies were scored as per Brunt et al. (1999), by two pathologists independently, without knowledge of clinical and laboratory data. Univariate analysis using Kruskal-Wallis, Mann-Whitney and Pearson  $\chi^2$  tests and multivariate logistic regression analysis controlled for the effect of age and gender was performed.  $P$  value  $< 0.05$  was considered statistically significant.

**Results:** Fifty-four (76.1%) patients were male and 17 (23.9%) females. Mean age was  $34.9 \pm 8$  yrs. Mean BMI was  $25.7 \pm 1.9$  Kg/m<sup>2</sup>. None had manifest obesity (BMI  $\geq 30$  kg/m<sup>2</sup>). Mean waist: hip ratio was higher in males ( $0.96 \pm 0.07$ ) than females ( $0.95 \pm 0.07$ ). Mean AST was  $67.9 \pm 25$  IU/L and ALT was  $106.9 \pm 42$  IU/L. Five (7%) patients had diabetes mellitus. Insulin resistance (HOMA-IR  $> 3$ ) was present in 42 (59.15%) hypertriglyceridemia in 62 (87.3%) and hypercholesterolemia in 11 (15.5%) patients. On necroinflammatory grading, 21 (29.6%) patients had grade 1, 26 (36.6%) grade 2 and 24 (33.8%) grade 3, NASH. Forty-three (60.6%) patients had stage 1 fibrosis. None had stage 4 fibrosis (cirrhosis). On multivariate analysis independent predictors of necroinflammatory grade were BMI ( $P = 0.009$ ), waist circumference ( $P = 0.035$ ), waist: hip ratio ( $P = 0.011$ ) and AST level ( $P = 0.000$ ); ( $R^2 = 0.52$ ). Independent predictors of fibrosis stage were female gender ( $P = 0.02$ ), cholesterol levels ( $P = 0.048$ ) and LDL levels ( $P = 0.025$ ); ( $R^2 = 0.38$ ).

**Conclusion:** NASH should no longer be considered a disease of obese, diabetic or hyperlipidemic females. It can present at a young age, in males, who may be asymptomatic, non-obese and non-diabetic. Female gender, BMI, waist: hip ratio, AST, hypercholesterolemia and increased LDL are independent predictors of disease severity in patients with NASH.

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### Venous Thromboembolism in Patients with Cirrhosis

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**Purpose:** It is the general notion that cirrhotic patients do not suffer from DVT/PE as they are naturally anticoagulated. However, there are no studies that objectively addressed if patients with cirrhosis have lower frequency of venous thromboembolism (VTE). Therefore, we conducted a case-control study to examine the relationship between cirrhosis and VTE.

**Methods:** A case-control study of patients seen at Wishard Hospital between 1995–2005 was performed using the Regenstrief Medical Record System. Cases were defined as hospitalized patients with biopsy and/or imaging plus clinical evidence of cirrhosis. Age, gender, and race-matched patients with no known evidence of cirrhosis seen during the same time period served as controls. The development of VTE was identified by the ICD-9 codes followed by cross referencing studies with Doppler ultrasound, V/Q scan, and CT chest. Subjects previously hospitalized with VTE were excluded. Charlson Index was calculated to determine the comorbidity. Patients with cirrhosis were also compared to age, gender, race, and Charlson Index matched non-cirrhotic patients with other chronic illnesses including chronic kidney disease (CKD), congestive heart failure (CHF), and five most common cancers in the US. Logistic regressions were performed to identify variables with predictive value.

**Results:** This study consisted of 963 cirrhotics ( $51 \pm 11$  yrs, females 34%, and Caucasians 60%) and 12,405 controls ( $51 \pm 11$  yrs, females 36%, and Caucasians 60%). Patients with cirrhosis had VTE (1.8%) and this is significantly higher than the controls (0.9%, OR: 1.78,  $P = 0.007$ ). The Charlson Index in cirrhotic patients was higher than that in controls ( $3.2 \pm 1.8$  vs.  $0.9 \pm 1.5$ ,  $P < 0.001$ ). However, in the combined cohort, cirrhosis (OR 0.87, 95% CI 0.2–2.6) and Charlson index (OR 0.93, 95% CI 0.74–1.16) were not independently associated with VTE. PTT (OR 0.88: 95% CI 0.84–0.94) and serum albumin (OR 0.47, 95% CI 0.23–0.93) were the independent predictors of VTE in the entire cohort. The risk of VTE in cirrhotics was much lower than those with other medical illnesses: 7.1% in CKD (OR 0.25;

95% CI 0.15–0.41), 7.8% in CHF (OR 0.23, 95% CI 0.14–0.37), and 6.1% in cancers (OR 0.29, 95% CI 0.17–0.52).

**Conclusion:** Underlying cirrhosis seems to be protective against VTE when compared to other chronic illnesses. However, patients with cirrhosis do not have lower risk of VTE compared to non-cirrhotic controls. PTT and serum albumin were independent predictors of VTE in cirrhotic patients.

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### Pathophysiology of Jaundice in Amoebic Liver Abscess

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**Purpose:** Jaundice in patients with amoebic liver abscess is a frequent occurrence. However, pathophysiology of jaundice in these patients is not fully understood. Hepatic necrosis leads to damage to bile ducts as well as various vascular structures leading to biliovascular fistula and jaundice. We studied mechanism of jaundice in patients with amoebic liver abscess.

**Methods:** We prospectively evaluated 10 patients with amoebic liver abscess with jaundice from February 2002 to January 2007. All patients underwent various investigations including imaging studies.

**Results:** There were 9 males and 1 female patient with a mean age of 39.1 years. Mean duration of illness before presentation was 13.1 days. All patients had fever and jaundice. We detected damaged hepatic veins and bile ducts in all patients with amoebic liver abscess causing biliovascular fistula and hyperbilirubinemia which reverted back to normal after biliary diversion with nasobiliary drainage.

**Conclusion:** Jaundice in patients with amoebic liver abscess is due to biliovascular fistula resulting from hepatic necrosis leading to damage to bile ducts and hepatic veins.

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### Cytokeratin 18 Levels as a Noninvasive Biomarker for Nonalcoholic Steatohepatitis in Bariatric Surgery Patients

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**Purpose:** Nonalcoholic fatty liver disease (NAFLD) is extremely common among patients undergoing bariatric surgery. Liver disease may progress in these patients despite surgical weight loss. Previously, we demonstrated that plasma concentration of cytokeratin 18 (CK-18) fragments accurately differentiated NASH from simple steatosis and was predictive of stage of fibrosis in patients with NAFLD. The aim of this study was to assess the usefulness of this biomarker in determining NASH in the bariatric surgery population.

**Methods:** Our cohort consisted of 99 consecutive patients who underwent liver biopsy at the time of bariatric surgery. Of these, CK-18 levels were measured in 86 patients who had plasma available within one week prior to surgery using a sandwich immunoELISA specific for CK-18 fragments. Histology was scored by experienced hepatopathologists according to the NAFLD NIDDK activity score.

**Results:** Plasma levels of CK-18 fragments ranged from 103 to 1000 U/L (Median (Q25, Q75): 226 U/L (177, 298)). Compared to either subjects with no NAFLD, simple steatosis or borderline diagnosis, CK-18 levels were significantly higher in subjects with NASH (median (Q25, Q75): 196 (158, 245) vs. 217 (154, 228) vs. 200 (176, 274) vs. 389 (275, 839), respectively;  $P <$

0.0001). CK-18 levels were significantly higher in subjects with moderate to severe fibrosis than in those with mild fibrosis (median (Q25, Q75): 334.5 (240.5, 896) vs. 207 (175, 275), respectively;  $P = 0.007$ ). For every 50 U/L increase in the plasma level of CK-18, the likelihood of having NASH as opposed to simple steatosis increased 2.45 times (OR (95% CI): 2.45 (1.20, 5.00)). The area under the ROC curve was estimated to be 0.88 (95% CI: 0.77, 0.99). The values with the best combination of sensitivity and specificity were 252 U/L (sensitivity = 82% and specificity = 77%) and 275 U/L (sensitivity = 77% and specificity = 100%).

**Conclusion:** These results demonstrate that determination of CK-18 fragments in the blood accurately differentiates NASH from simple steatosis and predicts stage of fibrosis in bariatric surgery patients, supporting the potential usefulness of this test in clinical practice as a noninvasive NASH biomarker.

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### Dysphagia from Hepatocellular Carcinoma Metastases to the Esophagus Occurring Post-Liver Transplantation

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**Purpose:** Introduction: Hepatocellular carcinoma (HCC) commonly metastasizes to the lungs, lymph nodes, musculoskeletal system and adrenal glands. Metastasis to the esophagus has been reported on rare occasions, though the diagnosis is usually made at autopsy. Esophageal metastases of HCC are thought to occur through tumor invasion into the portal system with subsequently dissemination. We present a rare case of symptomatic HCC metastasis to the esophagus occurring post-liver transplantation.

**Case:** A 71 year-old male was referred after evaluation of abnormal liver tests revealed an alpha-fetoprotein of 4,271 and a 6.5 cm mass in right lobe of liver suspicious for HCC. There was no personal or family history of liver disease or HCC, there was no weight loss or history of variceal bleeding, and examination revealed no signs of decompensated liver disease.

He was not a candidate for partial hepatectomy because the non-tumor part of the liver appeared cirrhotic on imaging. He underwent extended-criteria orthotopic liver transplantation about three weeks after his initial consultation. Explant pathology revealed moderately-well differentiated HCC in right lobe with small tumor nodules in left lobe. Surgical margins were positive for HCC at the portal vein and inferior vena cava margins. The non-neoplastic liver showed minimal steatosis and fibrosis.

Post-transplant course was complicated by liver abscess eventually requiring re-transplantation, abdominal pain after t-tube removal, and ERCP without obvious bile leak but with abnormal nodules seen in distal esophagus. He also developed nausea and dysphagia to solids. EGD revealed multiple pedunculated, ulcerated lesions in mid-distal esophagus, each 1–2.5 cm in size occurring alongside of varicose veins. Biopsied were consistent with HCC.

**Discussion:** Pre-mortem diagnosis of HCC metastases to the esophagus is extremely rare, but has been reported to occur similarly to our patient with clinical presenting symptoms of dysphagia and findings of pedunculated lesions in the esophagus. Our patient was at high risk for HCC recurrence or metastasis given the positive surgical margins. We believe this is the first reported case of pre-mortem diagnosis of HCC metastasis to the esophagus post liver transplantation.

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### Limited Value of Leukocyte Esterase Reagent Strips for the Quick Diagnosis of Spontaneous Bacterial Peritonitis

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**Purpose:** The goal of this study was to determine the reliability of leukocyte esterase (LE) reagent strips in diagnosing spontaneous bacterial peritonitis (SBP) in the inpatient and outpatient settings.

**Methods:** One hundred ten patients who underwent a diagnostic or therapeutic paracentesis were enrolled in the study. Paracentesis was carried out in the medical ward or outpatient clinics by interns, residents, or faculty attending physicians. The procedures were done in the usual fashion and sent for studies as dictated by the ordering physician. The Multistix<sup>®</sup> leukocyte esterase reagent strip test was performed at the bedside or examining table. The reagent strip was read by the proceduralist who recorded the results. The results of the reagent strips were then compared to the laboratory results. SBP was diagnosed when there was either an ascitic fluid PMN count  $> 250/\text{mm}^3$  or positive bacterial culture. The reagent strip scores (i.e. Negative, Trace, 1+, 2+, 3+) were recorded to determine the sensitivity, specificity, positive predictive value, and negative predictive value of diagnosing SBP.

**Results:** Seventeen of the 110 patients were diagnosed with SBP. Nine had neutrocytic ascites (PMN  $> 250/\text{mm}^3$ ) alone, 4 had positive cultures alone, and 4 had both neutrocytic ascites and positive cultures. Of these patients, only five had LE strip results of 1+ or higher (see table). When using 1+ or higher as the cut-off for positive or negative LE strips, the sensitivity was 29.4%, the specificity was 91.4%, the positive predictive value was 38.5%, and the negative predictive value was 87.6%. When using 2+ or higher as the cut-off for positive or negative LE strips, the sensitivity was 29.4%, the specificity was 97.8%, the positive predictive value was 71.4%, and the negative predictive value was 88.3%.

**Conclusion:** Contrary to previous reports, the reliability of using LE reagent strips to rapidly detect SBP was limited when different proceduralists perform the test. Thus, this study further illustrates the importance of obtaining a cell count and bacterial culture when assessing ascites.

LE Strip Results	SBP	No SBP
Negative	10	78
Trace	2	7
1+	0	6
2+	5	2
3+	0	0
Total	17	93

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### Zeaxanthin Reduces Fibrosis in a Gerbil Model of Non-Alcoholic Steatohepatitis

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**Purpose:** Non-alcoholic steatohepatitis (NASH) is characterized by fatty infiltration and inflammation, causing liver injury and fibrosis by inducing free radicals in the liver. Zeaxanthin is an anti-oxidant and carotenoid found in green leafy vegetables and melons. Zeaxanthin is preferentially distributed to the liver. We hypothesize that zeaxanthin supplementation may reduce the severity of NASH. In order to test this hypothesis, we established an animal model of steatohepatitis in Mongolian gerbils (the only known rodents able to absorb carotenoids from the gastrointestinal tract).

**Methods:** A methionine-choline deficient (MCD) diet, an established diet for the creation of steatohepatitis in other rodents, was utilized to induce steatohepatitis in Mongolian gerbils. A total of 24 weanling male Mongolian gerbils in 4 groups (6 gerbils in each) were utilized for this experiment. Three groups of experimental animals were fed for 6 weeks with the MCD diet ad libitum with gelatin-containing 12.5 mg/kg zeaxanthin (MCD12.5), or 25 mg/kg (MCD25) or no zeaxanthin controls (MCD0) (note: the MCD

diet >6 weeks led to gerbil mortality). A non-MCD control group was fed standard rodent chow ad libitum. Gerbils were euthanized and livers stained with hematoxylin and eosin (H&E) and trichrome.

**Results:** On H&E, all MCD gerbils developed significant liver steatosis with mild inflammation. No difference in steatohepatitis was observed between MCD12.5, MCD25, and MCDC groups. On trichrome, MCD25 gerbils had no fibrosis, MCD12.5 gerbils had minimal fibrosis, and MCDC gerbils had mild fibrosis. The non-MCD control group had no steatosis, inflammation or fibrosis.

**Conclusion:** This is the first model of steatohepatitis created in Mongolian gerbils, and the first controlled study using zeaxanthin to treat steatohepatitis. Zeaxanthin reduced fibrosis in our model of steatohepatitis. Zeaxanthin may protect the liver from developing liver fibrosis in steatohepatitis. Further studies are underway to fully evaluate the mechanism of zeaxanthin's antifibrotic properties in steatohepatitis.

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### Liver Transplant Patients with Hepatitis C Who Do Not Respond to Pegylated Interferon Plus Ribavirin Do Respond to Consensus Interferon Plus Ribavirin

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**Purpose:** Treatment of chronic hepatitis C remains a challenge because of poor responses to currently available drugs. For example, approximately 80% of patients with hepatitis C have genotype 1, and as many as 50% of these patients fail to show a sustained response to treatment with pegylated interferon (Peg-IFN) plus ribavirin (RBV). The aim of the present study was to examine the efficacy and safety of consensus interferon (C-IFN) plus RBV in patients with chronic genotype 1 hepatitis C who had failed treatment with Peg-IFN plus RBV.

**Methods:** Subjects were 8 patients with recurrent genotype 1 hepatitis C following liver transplant, who had either failed to respond or had relapsed after treatment with Peg-IFN plus RBV. Patients were treated with C-IFN (Infergen; 6–15  $\mu\text{g/day}$ ) plus RBV (400–1000 mg/day) for up to 52 weeks. Adverse events, serum chemistries, complete blood count and hepatitis C virus RNA (HCV RNA) was measured at baseline, 4, 12, 18, 24, 32, 48, and 52 weeks of treatment and 4, 12 and 24 weeks after completing treatment.

**Results:** Baseline HCV RNA was 41,200–74,700,000 IU/mL. Six of 8 patients responded to treatment with a 100-fold decrease in HCV RNA. Serum HCV RNA became undetectable in 4 patients and this response was maintained throughout their treatment ranging from 24 to 52 weeks, and in 1 patient for one month after stopping treatment. One patient failed to respond at 12 weeks and was discontinued. A second patient failed to respond at 4 weeks and was discontinued at 6 weeks because of proteinuria, increased serum creatinine and anemia. A third patient responded at 8 weeks, but was discontinued at 32 weeks because of severe dry skin. All 8 patients had an initial decrease in serum aminotransferases and bilirubin. Seven patients developed anemia (hemoglobin < 10 g/dL) and one patient developed neutropenia (absolute neutrophil count < 700/ $\mu\text{L}$ ). Anemia was treated satisfactorily with erythropoietin or a reduction in RBV, and neutropenia was treated satisfactorily with granulocyte colony stimulating factor or a reduction in consensus interferon.

**Conclusion:** A majority of liver transplant patients with hepatitis C who have failed to respond to Peg-IFN plus RBV show a substantial virologic response when they are subsequently treated with C-IFN plus RBV. Thus, C-IFN plus RBV represents a novel therapeutic option for patients with hepatitis C who do not respond to Peg-IFN plus RBV.

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### Prevalence and Predictors of Steatosis in Patients with Chronic Hepatitis C (HCV) Infection

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**Purpose:** HCV infection has been described as a risk factor for the development of steatosis and steatohepatitis. Steatosis has been associated with treatment failures in patients receiving combination therapy for HCV and with acceleration of fibrosis in chronic HCV patients. Few studies have assessed host and viral factors associated with the development of steatosis in HCV infection.

The aim of our study was to look at: i) The prevalence of steatosis in patients with chronic HCV infection. ii) Host and viral factors which are associated with steatosis

**Methods:** From January 2001 to November 2005, we retrospectively reviewed a cohort of 148 consecutive patients with chronic HCV who underwent liver biopsy. Data collected included age, race, gender, BMI, prior alcohol use, presence of diabetes, family history of diabetes, triglyceride level, cholesterol level, viral genotype and histopathologic findings on liver biopsy.

**Results:** Of the 148 patients with HCV in our cohort, 80 patients (54%) had steatosis. Mild steatosis was present in 45% and 9% of the patients had moderate or severe steatosis. Thirteen patients (9%) had cirrhosis. The mean BMI was  $27 \pm 5 \text{ kg/m}^2$ . Out of the 80 patients who had steatosis, 37 (46%) were females, and 43 (54%) were Caucasians. Upon univariate analysis, diabetes ( $P = 0.03$ ) and a BMI  $\geq 25 \text{ kg/m}^2$  ( $P = 0.005$ ) were significantly associated with steatosis in these patients with HCV infection. Race, gender, age and history of alcohol use were not significant. In multivariate analysis, BMI  $\geq 25$  ( $P = 0.01$ ) was the only factor associated with steatosis. Thirty-nine (49%) patients had viral genotype 1. Although steatosis was slightly more common in patients with genotype 3, no statistical difference in the presence of steatosis between the various genotypes was seen.

**Conclusion:** In earlier studies, steatosis has been described as an important risk factor for the severity of liver disease and nonresponse to therapy in patients with chronic HCV infection. Steatosis was present in 54% of our cohort of patients with chronic HCV infection. The primary risk factors for steatosis in chronic HCV infection were diabetes mellitus or BMI  $\geq 25 \text{ kg/m}^2$ . Further studies to determine if improved control of diabetes or weight loss prior to treatment of HCV improves response rates and the effect of these measures on progression to cirrhosis should be considered.

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### High MELD Score and Type of Immunosuppression Are Predictors of Gastrointestinal Bleeding after Liver Transplantation

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**Purpose:** Gastrointestinal bleeding (GIB) after liver transplantation is associated with significant morbidity and mortality. There is a paucity of information about the effects of various immunosuppression therapies on GI bleeding as well as the predictive value of the MELD score in GIB.

The aim of our study was to define the incidence, causes of GIB after liver transplantation, and to identify the clinical and demographic variables that are associated with GIB in post liver transplant patients.

**Methods:** The records of the 522 consecutive primary liver transplants performed at Albert Einstein Medical Center since January of 1995 to December of 2005 were reviewed retrospectively. A preliminary analysis examined the association among these variables and the complication of GIB after liver transplant patients. A logistic regression was used to determine the predictors of GIB after liver transplant patients.

**Results:** The incidence of GIB after liver transplant was 8.9%. The most common causes of bleeding after liver transplant were peptic ulcers 34.5%, followed by viral enteritis (CMV) (12.7%), portal hypertensive lesions (10.9%), anastomotic bleeds (4.5%), and other miscellaneous events.

A MELD score  $\geq 32$  prior to transplant statistically increases the risk (OR: 6.4; CI: 6.35–6.56;  $P < 0.001$ ), and immunotherapy with Tacrolimus decreases the risk of post transplant bleeding (OR 0.28; CI: 0.26–0.38;  $P = 0.001$ ). No other variables were associated with GIB post transplant. The presence of GIB after liver transplant is associated with a higher mortality.

**Conclusion:** Patients with MELD scores  $> 32$  are candidates for prophylaxis against post transplant GIB. Immunosuppression with Tacrolimus should be considered in these patients especially those with high MELD.

Logistic Regression Analysis			
	Odds Ratio	Confidence Interval	P Value
MELD $> 32$	6.42	6.35–6.56	$< 0.001$
TACROLIMUS	0.28	0.26–0.38	0.001

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### Severe Pulmonary Sarcoidosis Complicating Hepatitis C Therapy and Resolving after Treatment Withdrawal

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**Purpose:** Current treatment recommendations for hepatitis C include pegylated-interferon (PEG) and ribavirin (RVN). It is known that interferons can precipitate a variety of immune-mediated conditions. We describe a case of pulmonary sarcoidosis in a patient undergoing treatment for hepatitis C with PEG and RVN whose pulmonary compromise resolved after medications were discontinued.

**Case:** A 45-year-old African-American male presented with several weeks of dyspnea on exertion. He had a history of genotype 1 hepatitis C for which he was 24 weeks into treatment with PEG 180 ug SC qweekly and RVN 600 mg po bid. Physical examination revealed crackles throughout the lungs. Chest x-ray showed an increased interstitial pattern. Chest CT showed diffuse interstitial lung disease with a miliary pattern and bilateral mediastinal and hilar lymphadenopathy. PPD and histoplasmosis antibody were negative. An angiotensin converting enzyme level was elevated. The patient underwent a thorascopic lung biopsy which revealed noncaseating epithelioid granulomas with multinucleated giant cells. Special stains were negative. The patient was diagnosed with pulmonary sarcoidosis secondary to PEG  $\pm$  RVN as he had no findings to suggest preexisting disease. The patient was advised to stop taking his PEG and RVN and upon followup in pulmonary clinic six weeks later, he reported resolution of dyspnea. Hepatitis C viremia returned after treatment withdrawal.

**Discussion:** Interferons cause an exaggerated Th1-mediated immune response and the hepatitis C virus may serve as an antigenic trigger. The combination of PEG and RVN may further enhance the immune response to predispose patients to sarcoidosis. RVN monotherapy has not been implicated in the induction of sarcoidosis. This case illustrates that PEG/RVN can induce symptomatic pulmonary sarcoidosis and withdrawal of therapy without immunosuppressive treatment may be an effective treatment modality.

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### Factors Influencing Participation in Hepatitis C Research Trials

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**Purpose:** Blacks are disproportionately affected by HCV but have been underrepresented in clinical trials. The aim of this study was to examine factors that might impact willingness to participate in HCV trials.

**Methods:** Subjects with HCV were recruited from the Duke Liver Clinic and a primary care clinic in Durham, NC. Subjects were interviewed about attitudes to research. They also completed the Trust in Physician Scale, a validated measure of interpersonal trust in physician-patient relationships, and

the 5-item Duke Religious Index, a validated measure of the major dimensions of religiosity (public/organizational, private/non-organizational, and intrinsic religiosity). Chi square Analysis and Fisher's Exact test were used to assess categorical variables; continuous variables were analyzed using t tests for normal data and Wilcoxon Rank Sum test for non-normal data.

**Results:** The study group included 56 blacks and 24 whites with HCV. The table highlights that black subjects had lower education levels. Black subjects were less likely to have health insurance coverage and to have their own transportation. No differences were observed in trust or religiosity scales between blacks and whites. Black patients were less likely to enroll in a research study of an experimental medicine than whites (73.2% vs. 25%,  $P = 0.0002$ ). Blacks and whites were both likely to participate in a study of counseling or mental health treatment. Both groups were less likely to participate in a study with placebo (57% vs. 54%,  $P = 0.93$ ).

**Conclusion:** Black subjects with HCV are less likely to participate in studies of experimental medicines. Differences in trust and religiosity do not explain these preferences. Limitations in access to health insurance and transportation to clinics provide significant barriers to Blacks with HCV and may negatively influence participation in research activities.

HCV Patient Characteristics			
	Blacks	Whites	P value
Demographics	N = 56	N = 24	
Age, years (mean $\pm$ SD)	50.4 $\pm$ 6.9	50.3 $\pm$ 7.0	NS
Gender (% male)	51.8	50.0	NS
Education			0.0005
< grade 12	35.7	0	
High school graduate	39.3	45.8	
Some college/degree	25.0	54.2	
Insurance coverage			$< 0.0001$
Private/HMO	21.4	70.8	
Medicare	10.7	8.3	
Medicaid	39.3	12.5	
None	28.6	8.3	
Transportation			$< 0.0001$
Own car	35.7	79.2	
Others drive me	10.7	20.8	
Public transportation	41.1	0	

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### Can Metabolic and Hepatic Abnormalities Be Improved by Intra-gastric Balloon Treatment for Obesity?

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**Purpose:** In obesity, a cluster of metabolic alterations (Metabolic Syndrome, MS) is often associated with Fatty Liver (FL). The "bright liver" at abdominal ultrasonography (US) and, in most cases, increased levels of hepatic enzymes, alanine aminotransferase (ALT) and gamma-glutamyltranspeptidase (GGT), are considered the hallmarks of Nonalcoholic Fatty Liver Disease (NAFLD) in obese patients. Insulin resistance (IR) is the main link among obesity, FL and MS. Bioenterics Intra-gastric Balloon (BIB, Inamed Health, Santa Barbara, Ca., USA) is considered a safe procedure to prepare patients to the bariatric surgery. The aim was to evaluate if the weight loss induced by BIB can improve both IR and liver enzymes.

**Methods:** From March 2003 through April 2007 in our digestive endoscopy service, 100 patients (F 65; age 20–63 yrs) with obesity and severe obesity (BMI 32–62) underwent BIB insertion. The BIB was placed under endoscopic control and removed 6 months later. US, clinical and routine laboratory investigations were performed before and after BIB. IR was calculated by the Homeostasis Model Assessment (HOMA-IR), as fasting serum insulin ( $\mu$ U/ml)  $\times$  fasting plasma glucose (mmol/l)/22.5; values  $> 2.5$  indicate



a state of IR. Exclusion criteria: HBV(+), HCV(+), alcohol consumption >20 g/day, known drugs in the history.

**Results:** BMI decreased significantly after BIB ( $42.7 \pm 5.6$  vs.  $38.4 \pm 5.3$ ;  $P < .001$ ). BMI reduction higher than 10% ( $\Delta\text{BMI} > 10\%$ ) was observed in 50 patients (pts.). US showed FL in the majority (70%). In FL pts. ALT U/L ( $48.8 \pm 46.5$  vs.  $31.1 \pm 26.9$ ) and GGT U/L ( $41.5 \pm 38.9$  vs.  $29.5 \pm 20.9$ ) significantly decreased after treatment ( $P < .01$ ). In 30% pts. without FL at US (noFL), both ALT and GGT ranged normally before and after BIB. HOMA-IR basal values >2.5 were recorded in 86% FL and in 74% noFL pts. Values significantly decreased after treatment both in FL ( $6.03 \pm 4.47$  vs.  $4.21 \pm 3.35$ ;  $P < 0.05$ ), and in noFL pts. ( $4.71 \pm 2.62$  vs.  $2.89 \pm 1.39$ ;  $P < .001$ ). FL and noFL pts. with  $\Delta\text{BMI} < 10\%$ , HOMA-IR, ALT, GGT values did not significantly change after BIB. Before BIB in FL pts. a weak correlation ( $r = 0.37$ ) was found between GGT and HOMA-IR values. Hypertriglyceridemia in 42.3%, HDL cholesterol levels <40 mg/dL in 32.4% did not significantly change after BIB.

**Conclusion:** Weight loss induced by intragastric balloon reduces IR. The ALT and GGT decrease suggests an improvement of hepatic lobular inflammation. The benefit depends on a decrease of BMI higher than 10%. We confirm the pivotal role of IR in FL.

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### Retrospective Analysis of Treatment Outcome for Hepatitis C Genotype 4 in a Community Hospital

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**Purpose:** Studies on hepatitis C genotype 4 are scarce. The wide immigration movement makes it important to know about the less common genotypes in the US that are more prevalent in other geographic areas. We aim at analyzing the current approach and treatment results for patients with hepatitis C genotype 4.

**Methods:** Retrospective chart review to collect data on patients who were treated at our center for hepatitis C virus genotype 4 with Peg-Interferon and Ribavirin between Jan 02–Jan 07. Patients were identified from the laboratory logbook for all performed PCR testing. Analysis included patients who completed 48 weeks of treatment and 24 weeks of follow up.

**Results:** Out of 77 patients tested positive for Hepatitis C genotype 4, only 51 patients actually received treatment. After initiation of treatment, 30 patients (59%) achieved early virological response (EVR), while 5 (10%) did not (nonresponder). Fourteen patients (27%) stopped treatment due to un-tolerated side effects and 5 were lost for follow up. Twenty-seven patients completed 48 weeks of combination Peg-Interferon and Ribavirin all of whom had negative PCR at end of treatment. Sustained virological response (SVR) was achieved in 19 patients, 5 relapsed, and 3 lost for follow up. However when analyzing results according to treatment protocol (excluding the patients who were lost for follow up or withdrawn) the SVR was 19/29 (66%).

**Conclusion:** The SVR noticed in this study falls within the range of other reported studies about HCV genotype 4. The observed withdrawal rate was very high in this retrospective analysis. However, when patients tolerated and finished treatment their SVR seemed better than what is published for genotype 1.

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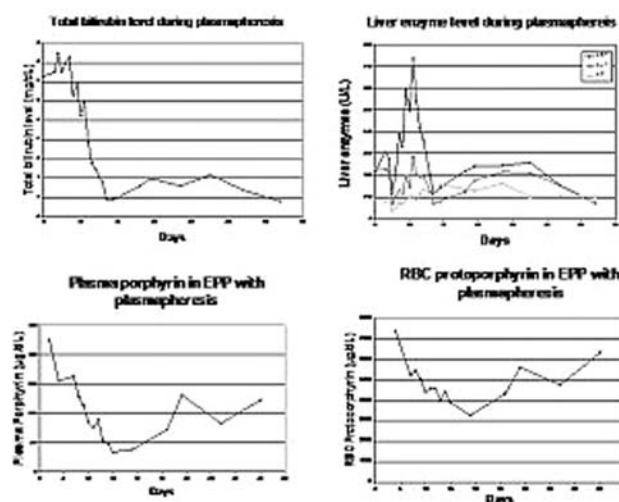
### Erythropoietic Protophyria (EPP) with Acute Hepatic Failure

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**Purpose:** Erythropoietic protoporphyria (EPP) is a genetic disorder of the heme synthesis due to deficiency of the enzyme ferrochelatase and is char-

acterized by overproduction of protoporphyrin, accumulation of protoporphyrin in liver results in hepatobiliary injury (cholestatic cirrhosis) and rapid increase may result in fatal acute hepatic failure. We report a case of EPP with cirrhosis presenting with acute liver failure managed successfully with plasmapheresis, hematin infusion and ursodeoxycholic acid. 17 year old female with history of photo sensitivity since childhood presented with jaundice, acute right upper quadrant pain, nausea and vomiting. Laboratory test revealed T Bil 8.5 mg/dl, Alk Phos 97, AST 736, ALT 283, Albumin 4, PT 23.7, PTT 30, INR 2.1, Platelet 82k, Viral Hepatitis serologies (A, B and C) were negative. Plasma porphyrins 224  $\mu\text{mol/L}$  and RBC protoporphyrins 7418  $\mu\text{mol/L}$  were elevated. Liver US revealed no biliary dilatation but cholelithiasis and hepatosplenomegaly. Liver biopsy demonstrated cirrhosis, and severe cholestasis. The liver protoporphyrin was 1287  $\mu\text{mol/gm}$ . Patient was diagnosed with EPP with acute liver failure and was treated with plasmapheresis and intravenous hematin infusion as well as cholestyramine and ursodeoxycholic acid. There was marked improvement in plasma porphyrins, RBC protoporphyrins, liver enzymes and total bilirubin. (Fig. 1). EPP presenting with acute liver failure liver is fatal and transplantation is the only option. Combined treatment with plasmapheresis, hematin, ursodeoxycholic acid and cholestyramine can stabilize the acute liver injury.[figure1]

### Clinical course of the patient with treatment



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### Tolerability of an Optimal PEG IFN Alpha + Ribavirin Regimen for Patients with Decompensated Liver Disease Due to Hepatitis C

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**Purpose:** To determine the tolerability of standard dosages of pegylated interferon alpha (PEG) and Ribavirin (RBV) in patients with HCV and decompensated liver disease.

**Methods:** A retrospective assessment of patients with HCV and decompensated liver disease treated with PEG and RBV initiated between 2002 and 2004. Demographic, virological data, and SVR were collected. Adverse events including further hepatic decompensation, medication dose reductions or discontinuations, depression, cytopenias and use of growth factors were documented.

**Results:** 16 patients with HCV and decompensated liver disease underwent therapy with PEG alfa-2b 1.5 mcg/kg/wk or PEG alfa-2a 180 mcg/wk and RBV 800 to 1200 mg daily. Male to female ratio was 14 to 2. 13/16 (81%) were Genotype 1. 75% were Caucasian. All patients had a history

of at least one of the following: variceal bleeding 7/16, ascites 9/16, hepatic encephalopathy 5/16, hypoalbuminemia 12/16. Three underwent liver transplantation during the initial 24 wks of therapy. Two discontinued therapy prematurely due to AE (interstitial pneumonitis, asymptomatic jaundice). Two developed significant ascites or hepatic encephalopathy. None had variceal bleeding. Four had worsening depression requiring the addition of or increase of anti-depressants. Although the majority developed cytopenias, only 4 required growth factors (3EPO/2 GSCF). Four required medication dose reductions. No patients obtained a SVR.

**Conclusion:** Standard dosage of PEG and RBV was reasonably well tolerated in selected patients with HCV and decompensated liver disease. 1) Few patients developed progression of liver disease or worsening of depression. 2) Expected rates of medication dose reduction/discontinuation were noted. 3) Cytopenias were common but manageable. 4) Larger prospective controlled trials are necessary to determine an accurate SVR for patients with HCV and decompensated liver disease who receive optimal dosing of PEG and RBV.

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**HBV Genotype in Northern Portugal**

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**Purpose:** Several factors including viral, host and environmental ones have been reported as determining the progression of liver disease in patients with chronic hepatitis B (HBV) infection. There is increasing evidence that HBV genotype may affect its clinical outcome and the response to antiviral therapy. Currently eight genotypes (A-H) of HBV are identified by a divergence of > 8% in the entire genomic sequence, and have distinct geographic and ethnic distributions.

We assessed the genotypic profile of HBV infection in Northern Portugal.

**Methods:** We have determined the genotypes and characterized the serological profiles of 97 patients. Genotyping was performed with conventional PCR with specific primers (as described by Naito, Hayashi and Abe, 2001). Sequencing DNA open gene with Tgene HBV Genotyping Kit (Bayer Healthcare) was used as confirmatory test.

**Results:** In 97 caucasian patients (61 men, 36 women), 70% were genotype D, 21% genotype A, 6% genotype F, 2% genotype E and 1% genotype C. Our major cohort of HBV infected replicative patients was HBeAg negative (77%). In both e-positive and e-negative patients, genotype D predominates (82% and 67%, respectively) but HBeAg positive patients only had genotype D and A, with large genotype variety in HBeAg negative patients.

**Conclusion:** In our HBV infected patients population, predominantly HBeAg negative, genotype D is the most prevalent (70%) along with a significant population of genotype A (21%).

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**Tumor Necrosis Factor (TNF)/Tumor Necrosis Factor Receptor (TNFR) Interactions Are Critical for the Development and Effector Functions of Hepatic and Splenic Cytotoxic T Cells in MHC Class I Disparate GVHD**

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**Purpose:** Graft-versus-host disease (GVHD) is increasing in patients who receive orthotopic liver transplants (OLTx) (1–2% of all OLTx). The mechanism of this life threatening disease is unclear, but several risk factors are considered to be important in its development. Murine models have been used to determine cause of GVHD. One murine model, in which the transfer of B6 T cells to MHC class I disparate bm1 × B6 F1 mice leads to the

development of hepatic GVHD. TNF inhibition, with an adenoviral vector expressing TNFR-Ig chimeric protein (Adv-TNFi) reduces GVHD pathological scores and hepatic CD8+, IFN- $\gamma$  producing T cells. The present studies were designed to determine the role of TNF on cytolytic (CTL) activity of responder spleen cells (SpC) and intrahepatic lymphocytes (IHL) from MHC class I disparate GVHD.

**Methods:** Allospecific killing of H-2<sup>bm1</sup> target cells by <sup>51</sup>Cr release assays (CTL assay) utilized SpC and IHL from sublethally irradiated bm1 × B6 F1 who received either B6 purified CD8+ SpC and T cell depleted BMC and control adenovirus (Adv- $\beta$ gal) or Adv-TNFi. In specific assays, TNF antibody (ab) or control ab (R & D Systems) was added at the beginning of the CTL assay. Levels of effector molecules from responder SpC from MHC class I disparate mixed lymphocyte culture (MLC) using B6 control or B6. TNFR1 –/– SpC and irradiated bm1 SpC were assessed by real time PCR.

**Results:** SpC from BMT recipients that had received Adv-TNFi displayed lower allospecific cytolytic activity than controls [(E:T 1:20 (77%) and 1:50 (80%) vs. 1:20 (13%) and 1:50 (17%)]. Addition of TNFR Ig further reduced allospecific killing during the cytolytic assay [(E:T 1:20 (45%) and 1:50 (47%) vs 1:20 (0%) and 1:50 (0%)]. IHL from BMT who had received Adv-TNFi had lower CTL activity than control BMT recipients [(E: T 1:20 (16%) and 1:50 (47%) vs 1:20 (0%) and 1:50 (4%)]. Of importance, the TNF antibody added prior to the CTL assay also decreased allospecific CTL activity against bm1 target blasts by IHL. Responder SpC from MHC class I disparate MLC using B6. TNFR1 –/– responder SpC displayed lower granzyme A, B and perforin expression than control B6 SpC (95%, 39% and 82% lower, respectively).

**Conclusion:** TNF/TNFR interactions are critical for CTL development and effector functions in SpC and IHL in MHC class I disparate GVHD.

## 303

**A Case of Hyperemesis Gravidarum**

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**Purpose:** Hyperemesis gravidarum is a clinical diagnosis that has no uniform criteria. The symptoms typically occur at four to ten weeks gestation. The diagnosis can be made in females with persisting emesis, weight loss greater than five percent of prepregnancy body weight and ketonuria beginning in the first trimester, as well as exclusion of other causes for these symptoms. A 64 year old G2P1 at 11 1/7 weeks gestational age with no significant past medical history was admitted to the medicine service for dehydration and hyperemesis. Patient complained of non-bloody emesis for the past month, occurring daily with no aggravating factors. The patient denied jaundice, diarrhea, bright red blood per rectum, arthralgias or skin rashes but noted she had a similar episodes of emesis with her last pregnancy that required hospitalization and resulted in elevated liver enzymes. Physical exam revealed a patient in no distress, anicteric sclera, abdomen was soft and nondistended with normal bowel sounds and no lower extremity edema. Lab workup revealed ALT of 1485 U/L, AST of 429 U/L, Alkaline phosphatase of 75 U/L, Potassium of 2.1 mmol/L, urine ketone of 150 mg/dl and normal platelets, hemoglobin and hematocrit.

In the hospital the patient was treated symptomatically for her nausea and emesis, given adequate intravenous hydration and vitamin supplementation. Further workup, including ANA, smooth muscle ab, Hepatitis panel, HIV, RPR, HSV IGM ab, CMV IgM ab and right upper quadrant ultrasound with doppler, were all negative. Throughout the patients hospitalization, her symptoms improved and her serum aminotransferases improved as well. After all lab work was obtained, the patient was diagnosed with hyperemesis gravidarum. The patient was then discharged home after she was tolerating po and had no complaints of nausea or emesis.

This case demonstrates when the diagnosis of hyperemesis gravidarum should be considered as well as how the diagnosis should be made. The diagnosis should be considered when persistent vomiting is accompanied

by weight loss exceeding five percent of prepregnancy weight and ketonuria that is unrelated to other causes.

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### Hepatic Fibrosis and Steatosis in Treatment Naive Chronic Hepatitis C Patients of Central California Valley

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**Purpose:** Liver biopsy is traditionally considered the gold standard to assess hepatic inflammation, fibrosis and steatosis in chronic hepatitis C (CHC) patients. This study assessed the severity of fibrosis and steatosis in liver biopsies of treatment naive CHC patients of Central California Valley.

**Methods:** We retrospectively evaluated 1031 consecutive CHC patients who underwent a percutaneous liver biopsy between years 2000–2006. Histology and steatosis were assessed with the METAVIR and Brunt scores respectively. Patients with coinfections and other liver pathologies were excluded from the study.

**Results:** Of 1031 patients, 566 (54.9%) were male and 465 (45.1%) were females. The mean age was 46 years; 46% being Hispanic, 46.8% Caucasian, 3.5% Afro-Americans and 1.8% Asians. The mean body mass index (BMI) was 29.97. AST and ALT levels and platelets counts were  $66.13 \pm 8.0$  U/L and  $78.9 \pm 8.0$  U/L and  $204.5 \times 10^9$  /L respectively. METAVIR F0-F1 was noted in 521 (50.9%) patients, 234 had F2 (22.8%), 270 had F3-F4 (26.3%) (Table). Brunt steatosis scores of 0, 1, 2 and 3 were observed in 44.1%, 39.6%, 12.6% and 3.7% of patients respectively. About 80.3% of patients were genotype 1; among these 42% had low and 18.8% had high steatosis scores.

**Conclusion:** The majority of CHC treatment naive patients in the Central California Valley had early fibrosis (F1-F2) and some degree of steatosis at the time of biopsy. Severe fibrosis was noted in one fourth of patients at the time of histologic diagnosis. There was a high prevalence of steatosis in CHC patients, particularly with genotype 1. Further studies are needed to evaluate the impact of steatosis on the clinical course and treatment response in CHC patients.

Baseline histology (METAVIR/Brunt scores)					
N = 1031	0	1	2	3	4
Fibrosis # (%) N = 1025	180 (17.6%)	341 (33.3%)	234 (22.8%)	155 (15.1%)	115 (11.2%)
Inflammation # (%) N = 1020	15 (1.5%)	253 (24.8%)	493 (48.3%)	239 (23.4%)	20 (1.96%)
Steatosis # (%) N = 820	362 (44.1%)	325 (39.6%)	103 (12.6%)	30 (3.7%)	—

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### Frequency of Hepatitis B Core Antibodies in Chronic Active Hepatitis C Patients in a Pakistani Cohort

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**Purpose:** The prevalence of Hepatitis C in Pakistan is about 4% and Hepatitis B is 2.5–3%. Estimated community burden is about 11 million people countrywide. As there was no mass immunization program before 2003 in the country, therefore, many patients of Hepatitis C had past exposure to Hepatitis B and recovered uneventfully.

**Setting:** Gastroenterology & Hepatology Division of Department of Medicine at Holy Family Hospital Rawalpindi – Pakistan.

**Study Design:** Retrospective observational study

**Methods:** PCR positive chronic hepatitis C patients were evaluated for Anti HBc in their serum. Other patients, who were reactive for HBsAg, excluded from the study. The information was recorded in a prescribed proforma; variables studied were patients age, gender, alanine aminotransferase level (ALT), and Anti HBc status. Anti HBc was done by ELISA third generation while HCV RNA was done by Roche Real Time. The data was analyzed using SPSS version 13.

**Results:** Out of 241 patients 116 (46.89%) were male and 125 (53.11%) were female. Mean age was  $38.05 \pm 13.37$ . Mean ALT level was  $70.97 \pm 19.58$ . Overall frequency of antibodies to Hepatitis B core antigen was 128/241 (53.11%) while in male it was 58/116 (50%) and in female it was 70/128 (54.68%).

**Conclusion:** Hepatitis B Core Antibodies has high frequency in Chronic Active Hepatitis C patients. Therefore, it is recommended that all patients undergoing investigation and treatment for HCV should be checked for Anti HBc of past exposure to HBV infection particularly in endemic area like Pakistan.

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### <sup>13</sup>C Breath Tests as Tools for the Assessment of Liver Diseases

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**Purpose:** It has been difficult to decide the pathogenesis of liver diseases accurately. <sup>13</sup>C breath tests are proposed as tools for the assessment of liver function and have a great advantage of various <sup>13</sup>C-substrate used. Therefore, different metabolic pathways can be examined by breath tests. Through a combination of several kinds of breath tests, we evaluate the efficacy of breath tests to differentiate fatty liver diseases (FLD) from chronic viral hepatitis (CH).

**Methods:** <sup>13</sup>C-acetate, <sup>13</sup>C-phenylalanine, <sup>13</sup>C-caffeine, and <sup>13</sup>C-valine breath tests were performed in 23 chronic liver diseases (mean age 67 years) in a crossover manner. The cause of liver disease was hepatitis C virus (HCV) in 8 patients, hepatitis B virus (HBV) in 3, and primary biliary cirrhosis in 1, alcoholic liver disease (ALD) in 4, non-alcoholic fatty liver disease (NAFLD) in 6. The patients received 100 ml of water containing 100 mg of <sup>13</sup>C-substrate in the sitting position after an overnight fast. Breath samples were collected at baseline and at 10 min-intervals for 150 min after ingestion to analyze <sup>13</sup>CO<sub>2</sub>.

**Results:** The <sup>13</sup>CO<sub>2</sub> concentrations increased from the beginning, and peak enrichment values were reached at 20 min after administration of <sup>13</sup>C-acetate. A peak value of CO<sub>2</sub> excreted was lowest in ALD (19.1 per mil), followed by NAFLD (21.1 per mil), and CH (48.9 per mil). After administration of <sup>13</sup>C-phenylalanine, <sup>13</sup>CO<sub>2</sub> excretion peaked at 30 min and the peak value was significant lower in FLD than in CH regardless of the serum albumin level and the platelet count. There were no significant differences in <sup>13</sup>CO<sub>2</sub> excretion after administration of <sup>13</sup>C-caffeine between FLD and CH. <sup>13</sup>CO<sub>2</sub> excretion in the first 60 min was significant lower in FLD than in CH after administration of <sup>13</sup>C-valine. <sup>13</sup>CO<sub>2</sub> excretion at 30 min is closely associated with the platelet count and the serum albumin level.

**Conclusion:** <sup>13</sup>C-acetate breath test is a useful non-invasive tool for distinguishing between patients with FLD and those with CH. <sup>13</sup>C-valine is the optimal stable isotope for the assessment of liver function although it is unable to differentiate FLD from CH.

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### Liver Histological Features of Randomly Selected Population with Abnormal Liver Sonography in Iran

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**Purpose:** Non alcoholic steatohepatitis is a world wide public health problem with no clinical symptom which is in doubt during a random liver enzyme tests and diagnosed by liver biopsy. This study was down to determine the Liver histological features of randomly selected population with abnormal liver sonography in Iran.

**Methods:** Total of 216 randomly selected non alcoholic subject with ultrasonographic fatty liver and no serologic markers of viral or autoimmune hepatitis and no findings in favor of metabolic liver disease were enrolled the study in Tehran.

Questionnaire, physical examination, serum biochemical liver tests was completed for all subjects. For those with persistent liver enzyme elevation and moderate or more sonographic fatty liver even without liver enzyme elevation, liver biopsy was performed. Analysis of data was down through SPSS 13 windows statistical package.

**Results:** 14.06% of subjects had liver enzyme elevation in addition of ultrasonographic fatty liver and 2.031% had moderate or more sonographic fatty liver without enzyme elevation. Both of these two groups were biopsied. Liver biopsy showed definite steatohepatitis (NASH Activity Score (NAS) 5 or more) in 66.66% and possible steatohepatitis ( $2 \leq \text{NAS} \leq 4$ ) in 33.33%. Steatosis in 33.33% was panacinar and in others azonal. 50% had microvesicular steatosis. 33.33% had moderate perisinusoidal/pericellular fibrosis. 66% had portal fibrosis. Microgranuloma and vacuolated nuclei were seen in 50% and 88.33% respectively.

**Conclusion:** Non alcoholic steatohepatitis must not be considered a disease restricted to specific groups only and its impact might be larger than what is generally considered. People may have considerable sonographic or histologic fatty liver in spite of normal liver enzyme tests.

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### Non-Invasive Predictors of Large Varices in Patients Hospitalized with Gastroesophageal Variceal Hemorrhage

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**Purpose:** To identify non-invasive factors predicting the presence of large varices (LV) in patients hospitalized with gastroesophageal variceal hemorrhage (GOVH).

**Methods:** Case records of patients admitted with GOVH between January 1998 to June 2005 were retrospectively analyzed. Relevant clinical parameters assessed included Child-Pugh class, clinically detectable ascites, portosystemic encephalopathy (PSE), clinically detectable splenomegaly and hemodynamic instability, as defined by Baveno. The laboratory parameters assessed were: hemoglobin, platelet count, prothrombin time, serum bilirubin, and albumin. The ultrasonographic characteristics noted were bipolar splenic diameter, presence of splenomegaly, presence of splenic varices, ascites and portal vein diameter. All patients with GOVH were included, and were divided into 2 groups based on the size of the esophageal varices (EV), which were classified as small (SV) or large (LV). Patients with gastric varices without (EV) were excluded.

Data were analyzed using SPSS. Variables with a  $P$  value of  $<0.25$  on univariate analysis were included in step-wise multiple logistic regression analysis to identify independent risk factors for LV, with  $P$  values  $<0.05$  taken as significant.

**Results:** A total of 420 patients presented with GOVH during the study period. The mean age, gender distribution, and frequency and etiology of cirrhosis were similar in the two groups. Liver cirrhosis with hepatocellular carcinoma (HCC), Child-Pugh class C, clinically detectable ascites, grade 3–4 PSE, detectable splenomegaly, previous history of GOVH, hemodynamic instability and platelet count  $< 91000$  were more common in the LV group. The frequency of radiologically detected ascites, splenomegaly and portal vein diameter were similar in both groups. On multivariate analysis, independent predictors for the presence of LV were: Cirrhosis with HCC ( $P = 0.029$ ), clinically detectable splenomegaly ( $P = < 0.001$ ), hemodynamic instability ( $P = 0.031$ ), a previous history of GOVH ( $P = < 0.001$ ), platelet count  $< 91000$  ( $P = < 0.001$ ), and splenic size  $\geq 158$  mm ( $P = 0.006$ ).

**Conclusion:** Cirrhosis with HCC, clinical splenomegaly, hemodynamic instability, a previous history of GOVH, thrombocytopenia  $< 91000$ , and splenic size  $\geq 158$  mm are independent non-invasive predictors of large varices in patients with gastroesophageal variceal hemorrhage.

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### N-butyl-2-cyanoacrylate in Gastric Variceal Bleeding – A Study To Determine the Short and Long Term Efficacy of This Agent

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**Purpose:** Catastrophic bleeding from Gastric varices (GV) occurs in 20% of patients with portal hypertension, either alone or in combination with esophageal varices. Injection of fundal varices with *N-butyl-2-cyanoacrylate* (a tissue adhesive) has been used with varying success in this setting. The data on the long term efficacy of this modality is very limited.

**Objective:** 1) To study the short and long-term efficacy of *N-butyl-2-cyanoacrylate* in control of fundal variceal bleeding. 2) To determine the optimal technique and amount of tissue adhesive to be used in this setting.

**Methods:** This Cohort type of interventional study was conducted in a Tertiary care referral center. Patients presenting with haematemesis and melena who were found to have fundal varices as source of bleeding were included. *N-butyl-2-cyanoacrylate* and lipiodol were injected into the gastric varices at EGD. Patients were followed six monthly for one year or longer after endoscopy for rebleed or mortality.

**Results:** The study population included a total of 56 patients with M/F ratio of 0.8; predominant age group of 40–59 years. GOV-2 and IGV-1 were seen in 2/3 and 1/4 of patients respectively. Almost 2/3 of the patients (59%) also had esophageal varices with high-risk stigmata. The average amount of *N-butyl-2-cyanoacrylate* used was 1 cc. Good hemostasis was noted at initial injection in more than 90% of patients while bleeding leading to haemodynamic instability was noted in 5 patients. Follow up for 1 year was possible in 36 patients; clinical and demographic variables were comparable in both these groups. 6 (17%) out of the 36 patients with long-term follow up ( $> 1$  yr) had rebleeding which was treated with re-injection or band ligation. Overall mortality was 4(11.1%) with half of this due to rebleeding from gastric varices. The overall rate of rebleeding at one year was 17% which is comparable to several other studies. However the average amount of *N-butyl-2-Cyanoacrylate* used in our study was significantly lower resulting in cost-savings.

**Conclusion:** 1) *N-butyl-2-cyanoacrylate* is a safe and effective mode of treatment for the short and long-term control of gastric variceal bleeding. 2) Smaller amounts of *N-butyl-2-cyanoacrylate* may be used with excellent efficacy in settings where cost remains a concern. 3) Most cases of rebleeding may be treated safely with *N-butyl-2-cyanoacrylate*.

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### Screening, Diagnosis and Treatment Strategies Used by the Gastroenterologists in Ohio for NASH/NAFLD

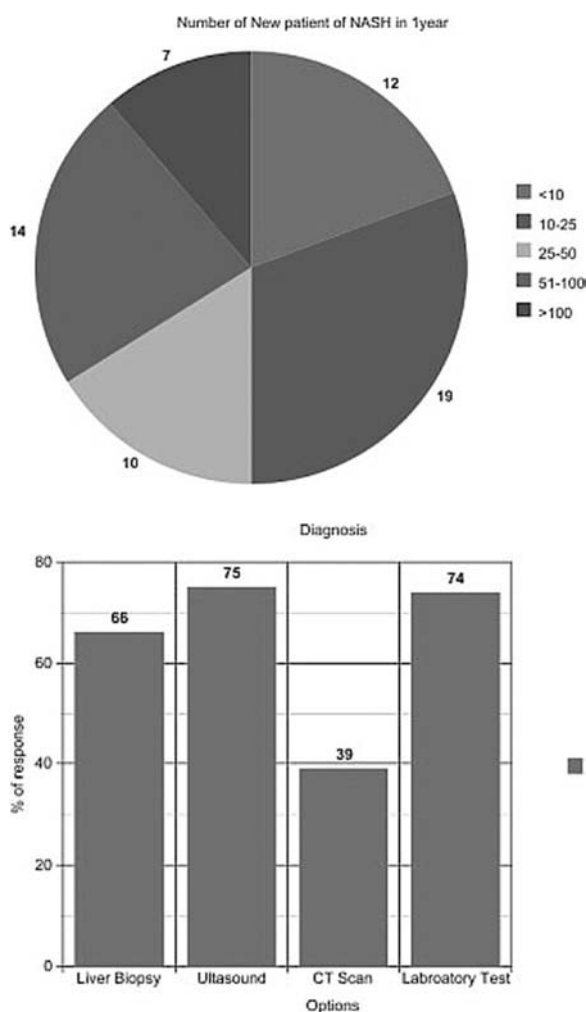
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**Purpose:** Fatty liver disease is now the most common cause for elevated liver function tests in the United States. Nonalcoholic steatohepatitis (NASH) is a progressive form of nonalcoholic fatty liver disease (NAFLD) that can lead to hepatic fibrosis and cirrhosis. As there is not enough data to effectively diagnose and treat NASH, this study evaluates trends of gastroenterologists in Ohio on their strategies in dealing with this rapidly escalating disease.

**Methods:** After approval from the institutional review board (IRB), questionnaire was sent to all 230 gastroenterologists practicing in Ohio. The content of the questions included methods of diagnosis, number of patient diagnoses in a year and treatment strategies.

**Results:** Of the 230 gastroenterologists, 61 responded to the questionnaire (26% response rate). Almost 50% of the gastroenterologists diagnose more than 25 new patients every year in Ohio. Most of the gastroenterologists answered more than one option for screening and treatment. Liver ultrasound is used by 75% of the gastroenterologists as the primary modality for diagnosis followed by laboratory tests, biopsies and Computerized Tomography Scan. NASH patients are managed by conservative treatment without adding Thiazolidinediones, Metformin or Antilipidemic agent by 72% of the gastroenterologists.

**Conclusion:** On an average, 50% of gastroenterologists in Ohio see more than 25–50 new patients in one year. Gastroenterologists in Ohio uses liver ultrasound as the primary modality for diagnosis and currently use mostly



conservative treatment for NASH. The lack of specific guidelines regarding the treatment and diagnosis by AASLD Practice Guidelines Committee on May 24, 2002 is consistent with wide variation in diagnosing and treating NASH or NAFLD in Ohio.[figure1][figure2]

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#### The APRI Is a Fair Estimator of Fibrosis in NAFLD, and May Be Enhanced by the Use of Age

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**Purpose:** Nonalcoholic fatty liver disease (NAFLD) is increasing in prevalence. Many patients with suspected disease do not undergo liver biopsy. Since it is expensive and invasive, it would be useful if a hepatic fibrosis index could identify those patients most likely to have significant disease that might benefit from a biopsy. The AST/Platelet Ratio Index (APRI) has been shown to be useful in chronic hepatitis C, but there is little data on it in NAFLD.

**Methods:** We retrospectively reviewed the pathology database at our institution from January 1995 to September 2006 using the search keywords of "steatohepatitis" and "liver biopsy". Of the 318 patients identified, 210 were excluded because of a history of HBV, HCV, autoimmune hepatitis, or recent heavy alcohol use. Among the 108 remaining patients we recorded the AST, ALT, platelet count, demographic data, and when appropriate the liver biopsy slides were examined blindly. Liver biopsies were staged by F0-F4 criteria with patients with pericellular fibrosis only classified as F1. Mild fibrosis was defined as F0-F1 and significant fibrosis as F2-F4. The APRI was calculated as below.\*

**Results:** The number of patients by stages were F0 (17), F1 (42), F2 (22), F3 (8), and F4 (19). The AUC for the ROC curve for the APRI was 0.758 (95% CI 0.667–0.836). Using a cutoffs of  $\leq 0.44$  and  $\geq 1.0$  the APRI predicted 37 of 49 for mild fibrosis and 16 of 17 for a significant fibrosis for a NPV of 75.5% and a PPV of 91.4% respectively. Using logistic regression, and the APRI and age, we were able to construct a risk ratio. The AUC for the ROC for the APRI and age was 0.802 (95% CI 0.714–0.873). Using cutoffs of  $\leq 0.84$  and  $\geq 0.58$  this risk ratio predicted 32 of 39 patients with mild fibrosis and 22 of 23 patients with significant fibrosis for a NPV of 82.1% and a PPV of 95.7% respectively. The indeterminate zones were 38.9% for the APRI and 42.6% for the APRI and age.

**Conclusion:** The APRI is a fair estimator of fibrosis in NAFLD. It appears to be most useful in predicting significant fibrosis with a cutoff of  $\geq 1.0$ . It may be modestly enhanced by incorporating age. \*APRI =  $\text{AST/ULN} \times 100/\text{platelets}^9$

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#### Adequacy of Liver Biopsy Specimens Performed by Gastroenterologists and Radiologists

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**Purpose:** Liver biopsy is the gold standard to establish the severity of inflammation and fibrosis in chronic hepatitis C (CHC) patients. Specimens measuring 20 mm long are usually considered optimal to determine grade and stage reliably. This study looked at the adequacy of biopsy specimens performed by both gastroenterologists and radiologists at three Hospitals in the Central California Valley.

**Methods:** We retrospectively evaluated 1031 consecutive patients with CHC who underwent percutaneous liver biopsies between years 2000–06. The pathology reports and other clinical data were reviewed in detail. Biopsy

specimen size on cut sections and adequacy to interpret fibrosis staging was assessed.

**Results:** The study population included 566 (54.9%) male and 465 (45.1%) female patients; 46% being Latinos, 46.8% Caucasian, 3.5% Afro-Americans and 1.8% Asians. The mean age of patients was 46 years and mean body mass index (BMI) 29.9. The mean and median length of biopsy specimens obtained by radiologists (N = 682) was 14.58 and 15 mm and by gastroenterologists (N = 347) was 14.57 and 13 respectively ( $P = 0.983$ ). The majority of biopsies by radiologists were obtained by 14–20 G trigger (tru-cut) needles, while gastroenterologists predominantly used 16 G aspiration needles. Among the biopsies performed by radiologists 60% (N = 411) of patients were referred predominantly by primary care providers. Of 1031 biopsies, 15.8% (N = 163) were  $\leq 10$  mm in length; among these 65% were performed by radiologists and 35% by gastroenterologists. Fibrosis staging was reliably made by the pathologists in 84.2% of specimens measuring  $\geq 10$  mm.

**Conclusion:** The majority of liver biopsies on CHC patients in the Central California Valley are performed by the radiologists, regardless of BMI of patients. Among these, most biopsies did not meet the criteria for optimal length described in the literature. There was no significant difference in the biopsy specimens obtained by the gastroenterologists and radiologists. Specimens  $< 10$  mm were usually inadequate to accurately establish stage of fibrosis.

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#### Iron Reduction by Phlebotomy Reduces alpha Fetoprotein in Patients with Advanced Chronic Hepatitis C: A Long Term Follow-Up Study

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**Purpose:** Phlebotomy with iron depletion is known to lower transaminases in patients with chronic hepatitis C (CHC). We present the results of long term (up to 9 years) maintenance phlebotomy program in patients with advanced CHC, high AFP and proven cirrhosis or bridging fibrosis.

**Methods:** All 18 patients with CHC failed therapy with PEG-interferon/ribavirin. Liver biopsy showed cirrhosis in 13 patients and bridging fibrosis in 2 patients. 9 patients were African American. None of the patients demonstrated HFE mutations. Patients underwent phlebotomy with 300 ml to 500 ml removed every two weeks, with the intent to reduce ferritin while maintaining hemoglobin above 11.5. Liver enzymes, ferritin, hemoglobin, AFP

Average lab values at different time intervals pre and post phlebotomy					
Lab values	Values prior to phlebotomy	3 months PP	1 year PP	3 years PP	5 years PP
Hemoglobin	14.1 SD 1.4 (N = 18)	12.7 SD 1.3 (N = 14)	13.4 SD 1.4 (N = 16)	13.6 SD 2.0 (N = 11)	14.2 SD 1.2 (N = 6)
Ferritin	781 SD 610 (N = 17)	121 SD 130 (N = 11)	108 SD 88 (N = 13)	74 SD 68 (N = 10)	67 SD 30 (N = 6)
AFP	50 SD 54 (N = 18)	27 SD 16 (N = 10)	17 SD 14 (N = 15)	17 SD 18 (N = 10)	15 SD 7 (N = 5)

PP = post phlebotomy, SD = standard deviation

and platelets were recorded; we rounded to the nearest time interval with respect to the six-biochemical parameters. The (n) in table 1, for 3 months and 1 year is  $< 18$  because not all patients had labs done at those time points. Signs and symptoms for clinical decompensation were assessed.

**Results:** Average ALT, AST and AFP at 3 months, year 1, year 3, and year 5 were all significantly lower than baseline ( $P < 0.01$  for all except AST at 5 years,  $P = 0.025$ ) (Table 1). There was no significant difference seen in platelet count or hemoglobin. AFP dropped in all patients. Pre-phlebotomy AFP was  $> 40$  in 7 patients, none of these patients developed hepatoma over an average of 39 months. No patients developed: encephalopathy, refractory ascites, variceal bleeding or hepatoma.

**Conclusion:** In patients with CHC, high ferritin and high AFP, a maintenance phlebotomy program can lower AFP as well as transaminases, and maintain the low AFP long term, without inducing anemia. Despite a very high AFP at the start of the phlebotomy regimen, none of the patients developed a focal mass or clinical evidence of hepatoma or clinical decompensation. Maintenance phlebotomy and sustained iron depletion needs to be evaluated further as a strategy in patients with CHC cirrhosis who have failed anti-viral therapy.

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#### Cryptococcus and Cirrhosis. Have We Been Missing the Association?

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**Purpose:** Disseminated Cryptococcosis is a disease rarely seen outside the setting of profound immunosuppression such as post-transplant patients, Acquired Immune Deficiency Syndrome or malignancy. Less than 30 cases of systemic cryptococcal infection have been described in literature (1965–2006) in patients with no immunosuppressive conditions other than cirrhosis. We presented one of the cases in 2005 American College of Gastroenterology (ACG) annual meeting and within 18 months encountered another case. We hereby suspect that this is an underdiagnosed condition and postulate that cirrhosis per se could be a strong risk factor for disseminated cryptococcosis and high index of suspicion needs to be maintained to ensure early diagnosis of this serious entity.

**Conclusion:** Both the patients described in this case series had no other immunosuppressive condition other than advanced cirrhosis. The diagnosis was made after the peritoneal/blood cultures grew *Cryptococcus*. Slow growth of the fungus in cultures usually contributes to delayed (or missed) diagnosis and initiation of therapy leading to a poor outcome. A rapid and reliable screening test like cryptococcal antigen in serum and/or ascitic fluid would have resulted in prompt initiation of anti-fungal therapy. 1. Spontaneous cryptococcal peritonitis should be suspected in patients in atypical SBP like presentations. (Absent leukocytosis in ascitic fluid, clinical worsening despite antibacterial therapy, lymphocyte predominant leukocytosis). Disseminated cryptococcosis may be an underdiagnosed disease in cirrhotics. 2. Ascitic fluid and serum for cryptococcal antigen should be tested in above presentations. 3. Prospective trials to study the relevance of cryptococcal antigen testing in atypical SBP like presentations are needed.

Clinical characteristics of patients with Cryptococcosis

Patient Age/sex/Initial MELD	Underlying Condition	Presenting Symptoms	Ascitic Fluid analysis	Cryptococcal Cultures	Delay in diagnosis from initial presentation	Antifungal therapy	Outcome
43/Hispanic M/28	HCV cirrhosis and no other immunosuppressive condition	Abdominal Pain and Fever	WBC = 50 (14% segs & 56% lymphs)	Peritoneal fluid and blood	5 days	Amphotericin for one day	Anuric renal failure, hospice and death
58/Caucasian F/23	HCV cirrhosis and no other immunosuppressive condition	Abdominal pain and worsening ascites	WBC = 52 (23% segs & 30% lymphs)	Peritoneal fluid and blood	48 hrs	Amphotericin for 2 days	Renal failure, progressive coma and hospice

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**Autoimmune Hepatitis: A Risk Factor for Cryptogenic Cirrhosis**

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**Purpose:** The etiology of cryptogenic cirrhosis (CC) is poorly understood. It is recognized that a significant number of patients with CC may result from nonalcoholic fatty liver disease (NAFLD) yet its cause in the others remains unknown. Occult autoimmune hepatitis or toxic liver injuries have been the other proposed causes of CC. The aim of the present study was to identify the clinical, biochemical, immunologic and histologic parameters of autoimmune hepatitis (AIH) in patients with CC to ascertain whether AIH is a causative risk factor for the disease.

**Methods:** Thirty five consecutive patients who had liver transplant for CC were studied. Clinical, biochemical, immunologic and histologic parameters were analyzed and the International Autoimmune Hepatitis (IAH) score calculated. Explant histology was reevaluated by a hepatopathologist for the inflammation, lymphoid aggregate, plasma cells, interface hepatitis, steatosis, perivenular and sinusoidal changes, glycogenated nuclei, Mallory hyaline, bile duct changes, hepatocyte necrosis and fibrosis.

**Results:** The mean age of patients was  $53.7 \pm 13$  years, BMI was  $29.6 \pm 6.8$  Kg M<sup>2</sup> (range 21–42) and 57% were females. Diabetes was present in 42%; obesity in 63%, and 37% had concurrent illness. The liver chemistry revealed mild to moderate increase in aminotransferases (AST  $85.5 \pm 105$ , ALT  $67 \pm 70$ , AST/ALT  $1.4 \pm 0.6$ ) and Alk Phos ( $187.7 \pm 97.7$ ).

The ANA was positive in 17% and anti-smooth muscle antibody in 31%. Mean IAH score was  $7.0 \pm 3.0$  and a score of 10 or greater was seen in 14%. However, in 60% of the patients with the high IAH score, the histologic features of residual NAFLD were also present. Liver histology showed cirrhosis in all. No interface hepatitis or plasma cell infiltrates were seen. Varying grades of centrilobular sclerosis (27 biopsies) and sinusoidal fibrosis (18 biopsies) indicative of residual NAFLD were seen in addition to Mallory hyaline seen in 23%.

**Conclusion:** Occult or burnt-out AIH diagnosed by clinical, biochemical and immunologic criteria may be a risk factor leading to CC in a subset of patients. In some patients, dual injury from NAFLD and chronic AIH resulting in CC is a possibility. It remains conjectural that, the classic histology of AIH may be altered or lost once the disease progresses to cirrhotic stage.

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**34 Year Old Pregnant Female Presents with Abdominal Pain**

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**Purpose:** 34 year old female, gravida 4, para 0, at 16 weeks of gestation presented with abdominal pain for 3 days, epigastric/right upper quadrant, severe, with nausea and vomiting. Patient denied fever, arthralgias, or change in bowel habits. Her past medical history was significant for systemic lupus erythematosus without active manifestations and antiphospholipid antibody syndrome. She denied any history of smoking, alcohol use, or illicit drug use. Her medications included aspirin, enoxaparin, hydroxychloroquine, and prenatal vitamins. She was allergic to sulfa and penicillin. Physical exam revealed elevated blood pressure (150/84 mmHg), tenderness in right hypochondrium with voluntary guarding and a gravid uterus. Lab studies revealed thrombocytopenia, elevated transaminases (7 times above the normal value), LDH and decreased haptoglobin. Urinalysis revealed proteinuria with trace blood. Ultrasound of the abdomen revealed thickened gallbladder wall without gallstones. CT scan of the abdomen revealed densities throughout the liver consistent with hepatic infarctions/necrosis. Our patient was diagnosed with HELLP syndrome with hepatic infarctions/necrosis. Hepatic

infarction in pregnancy is a rare condition, with an estimated incidence of 1 in 40,000 to 250,000 pregnancies. The hepatic infarction although rare, usually occurs after the 20th week of pregnancy and usually involves the right lobe of the liver. The diagnosis is established by abdominal ultrasound, CT scanning, MRI or angiography. Hepatic rupture is a dangerous complication that can cause mortality rates as high as 85 percent. Treatment is generally limited to conservative management and delivery of the fetus. Our case is unique in that the patient presented with this clinical syndrome in the 16th week of her pregnancy and her hepatic infarctions included most of her liver and her medical history included antiphospholipid antibody syndrome. Less than 30 such presentations have been reported in our literature search. Our patient had an uncomplicated dilatation and evacuation procedure.[figure1]



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**Capsule Endoscopy Can Discriminate between Large/Medium Varices and Small or No Varices: Defining the Threshold**

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**Purpose:** Guidelines recommend surveillance endoscopy (EGD) in patients with portal hypertension. Risk of hemorrhage is correlated to variceal (EV) size and presence of endoscopic stigmata. Treatment is recommended when medium/large varices (M/LV) are present. Reports indicate that PillCam ESO (EC) is a sensitive tool for identifying M/LV when the varix comprises more than 25% of the circumference of the circular field view. We evaluated the ability of EC to discriminate small from M/LV using the current grading scale. In addition, we sought to identify a correlation between varix size by EC and endoscopic grade.

**Methods:** Patients underwent EC within 48 hours of EGD. A separate blinded investigator interpreted capsule findings for size of esophageal varices (M/LV if >25% of the lumen circumference is occupied; small if <25%, and absent if no EV detected), exact degree of circumferential occupation if EV present, signs of risk, evidence of prior banding and degree of portal hypertensive gastropathy (PHG).

**Results:** 20 patients underwent EC and EGD. One EC was excluded due to rapid esophageal transit time. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for EC as compared to EGD are shown in Table 1. The sensitivity of CE to identify M/LV was 22.2%. Reduction in the threshold for M/LV to 12.5% of the luminal circumference results in greater sensitivity, specificity, PPV, and NPV, see Table 2. CE detected risk signs in 4/9 cases. CE correctly identified PHG in 15/15 cases.

Four additional cases of PHG not seen on EGD were reported on CE. CE correctly recognizes 2/5 case with prior banding, did not identify 3 cases and was false positive in 1.

**Conclusion:** Our pilot study indicates that discriminating varices by the current capsule scale is unreliable. However, lowering the grading threshold improved the ability to discriminate size of EV on CE. EC is a good test for the detection of PHG. The weakness of CE is in detecting small varices but this is not of clinical significance. Future studies with larger sample size are required to further validate our results.[figure1]

Table 1

EC and the Ability to Detect the Presence of EV		Presence of EV on EGD	
		Yes	No
Presence of EV on EC	Yes	12	1
	No	5	1

- Sensitivity: 70.6%
- Specificity: 50%
- PPV: 92.3%
- NPV: 16.7%

Table 2

M/LV defined as 25% of luminal circumference				M/LV defined as 12.5% of luminal circumference			
		M/LV on EGD				M/LV on EGD	
		Yes	No			Yes	No
M/LV on CE	Yes	2	1	M/LV on CE	Yes	9	1
	No	7	9		No	0	9

- Sensitivity: 22.2%
- Specificity: 90%
- PPV: 66.7%
- NPV: 56.3
- Sensitivity: 100%
- Specificity: 90%
- PPV: 90%
- NPV: 100%

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### In Hospital Mortality Rates of Patients Admitted for Esophageal Variceal Hemorrhage over a 15 Year Period: MELD as a Predictor

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**Purpose:** To compare mortality rates amongst two cohorts of patients admitted for acute esophageal variceal hemorrhage and to evaluate predictors of in-hospital mortality.

**Methods:** Retrospective chart review of patients identified by ICD-9 codes for admission diagnosis of acute esophageal variceal hemorrhage (N = 73). Cohorts consist of patients admitted between 1990–1997 and 1998–2005. Data collected included demographic information, etiology of liver disease, admission MELD, treatment modalities (medical and mechanical therapies), and patient outcome (death, length of stay). Statistical Analysis was carried out using Fisher's exact test, student t-test and receiver operating characteristic curves.

**Results:** While mortality between cohorts did not significantly change, 37% for 1990–1997 vs. 29% for 1998–2005 ( $P = 0.758$ ), a MELD score greater than 15 had a sensitivity of 85% for inpatient mortality with an area under the receiver operating characteristic curve of 0.872 (95% CI: 0.763–0.981). On univariate analysis, mean MELD score of patients that died during admission vs. those that survived until discharge were 27 (SD 10) vs. 13 (SD 5), respectively. This difference in MELD was statistically significant with a  $P$  value < 0.001.

**Conclusion:** While MELD may not always reflect true severity of liver disease in individuals with cirrhosis-related complications, this study suggests that it may be a good prognostic tool in individuals who present with acute esophageal variceal hemorrhage.

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### Metformin Induced Cholangiohepatitis – An Uncommon Presentation

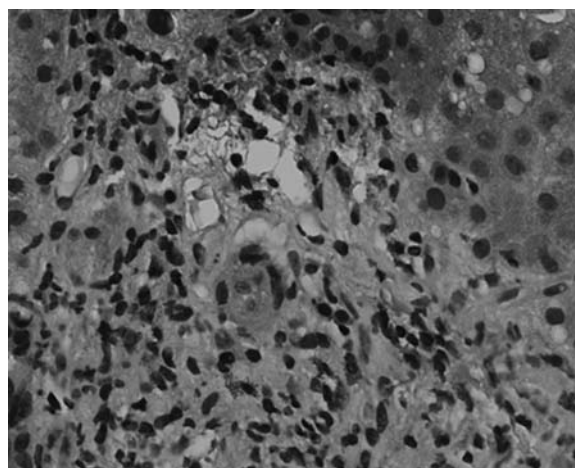
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**Purpose:** Metformin hydrochloride is an oral biguanide anti hyperglycemic commonly used in the treatment of type 2 Diabetes. It improves insulin sensitivity, decreases hepatic glucose production and increases glucose transport across skeletal muscle membrane. It is not metabolized by the liver and is excreted unchanged in the urine. The major side effects includes diarrhea, nausea, vomiting, bloating, flatulence and lactic acidosis. Here, we report a unique case of acute cholangiohepatitis with metformin use.

**Methods:** A 63 yr old male presented with fever, right upper quadrant abdominal pain, nausea and vomiting for 4 days. Metformin (500 mg oral twice daily) was added to his drug regimen four weeks before the onset of symptoms. His other medications included ASA, glyburide and allopurinol.

**Results:** Amylase, lipase and hepatitis serologies were negative. AST 38 IU/L, ALT 169 IU/L, alkaline phosphatase 437 IU/L, albumin 3.0 gm/dL and total bilirubin 4.2 mg/dL. Abdominal ultrasound showed mildly distended gallbladder with wall thickening with CBD at 5 mm. ERCP revealed absence of ductal dilatation or filling defects. HIDA scan showed delayed filling of the gallbladder suggesting chronic cholecystitis. Percutaneous liver biopsy demonstrated portal tracts with a mixed inflammatory infiltrate, characterized by lymphocytes, neutrophils and abundant eosinophils. Acute inflammatory cells were seen infiltrating bile ductules, with epithelial disruption and compensatory ductular proliferation. No portal or parenchymal bile stasis was noted. The histopathologic findings were compatible with mild subacute cholangitis and the presence of abundant eosinophils raised the possibility of medication associated cholangitis. Metformin was discontinued.

**Conclusion:** Continued elevation of alkaline phosphatase led to laparoscopic cholecystectomy and liver biopsy 6 weeks after the initial presentation. Biopsy showed moderate chronic portal triaditis with peice meal necrosis and stage 2 fibrosis consistent with residual medication effect. Currently his liver function tests are back to normal. This case highlights the importance of excluding drug induced hepatitis before undergoing cholecystectomy.[figure1]



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### Statins and Hepatitis C Therapy: A Retrospective Analysis in a Veteran Medical Center

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**Purpose:** Hepatitis C virus (HCV) may infect the hepatocytes through the interaction with CD81 receptors. LDL receptors may serve as coreceptors for the binding, entry, and internalization of HCV. Statins might be potential inhibitors for Hep C entry.

**Aim:** To evaluate the effect of Statins on the outcome of therapy in HCV infected patients and to assess its tolerability

**Methods:** We conducted retrospective electronic records review using the Hepatitis C Registry database at the VA Medical Center from January 2000 to October 2006. Patients with HCV who had completed at least 12 weeks of therapy with peginterferon and Ribavirin were included in the study. A subcategory of patients who were on concomitant therapy with Statins was emphasized.

Data collected: age, gender, ethnicity, BMI, Genotype, Pharmacy prescription utilization of Statins, Rebetrone, PEG interferon, and Ribavirin, the duration of therapy, ALT level pre and during Statins therapy, HCV PCR at 12 weeks, end of therapy and 6 months after HCV therapy. all follow up notes were reviewed as well.

**Results:** 125 patients who completed 12 weeks of therapy were included in the study. 8 patients (6%) were on statins, all patients of which had an early virological response (100%). 74 patients in the non-statin group (n 117) had an early virological response (64%). The difference was statistically significant ( $P$  value 0.0007). five patients in the statin group and 74 in the non-statin group completed 48 weeks of hepatitis C therapy. three patients (60%) had a sustained virological response (SVR) in the statin group. Twenty-four (32%) patients had an SVR in the non-statin group. There was a trend towards significance ( $RR = 1.756$ , 95% CI: 0.45 to 6.86). None of the patients in the statin group had an elevation of transaminases.

**Conclusion:** In this small sample study, the use of statins during hepatitis c therapy showed no worsening in liver enzyme. In fact, its use might improve early viral response to therapy. The limiting factor of using statins in HCV infected patients is the elevated Liver enzyme but no reported incidence of any complication in our study.

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#### A Case of Wilsons Disease with Fulminant Liver Failure

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**Purpose:** A 22-year-old white female was admitted with one month history of intermittent bloody diarrhea, increased in severity for four days prior to admission. Associated symptoms included sore throat, fatigue, abdominal bloating, fever, chills, nausea and vomiting bilious material. She also complained of recent onset dark, "smoky" urine and yellow discoloration. No history of pruritis, recent travel, blood transfusion, or easy bruising. On examination the patient had jaundice and was in slight discomfort, with a fever of 102.5 F. She was lethargic, but arousable and oriented to person, place and time. Abdomen was soft and non-tender; no guarding, or hepatomegaly appreciated. No signs of chronic liver disease. Rectal examination revealed dark brown stool. Laboratory examination indicated an elevated white count with bandemia, hemoglobin of 7.2 (MCV 112; RDW 14). BUN and creatinine were 45 and 2.8. Liver transaminases: ALT 17, AST 193 Alk Phos <3, Albumin 2.3 and Total bilirubin 19.3 (Direct 12.6). Coagulation profile showed INR 4.2 and PTT 55. Further evaluation demonstrated Coombs test negative hemolysis; spherocytes, nucleated RBC; left shift of WBC to promyelocyte stage; Plts 100,000 with large forms on peripheral smear. The patient was started on antibiotics for an initial diagnosis of infectious diarrhea. CT scan of the abdomen showed moderate ascites, splenomegaly, distended gallbladder and thickening of colonic wall. No liver lesions were noted. Based upon clinical suspicion a thorough ophthalmological evaluation was performed and revealed dark brown/yellow rings in the peripheral cornea of the deep stroma consistent with Kayser-Fleischer rings. The patient was referred for a liver transplant, which she received shortly thereafter. Wilsons disease is a rare autosomal recessive disorder of copper metabolism in which excess copper accumulates in the liver, central nervous system and

other tissues. The incidence is approximately 1 in 30,000 with most patients presenting between the ages of 5 and 40. Fulminant hepatic failure usually occurs in children or young adults not previously diagnosed with Wilsons disease. Our case demonstrates a challenging diagnosis based upon clinical suspicion and laboratory data consistent with fulminant hepatic failure in this disease: Coombs-negative hemolytic anemia, coagulopathy unresponsive to Vitamin K, rapidly progressive renal failure and a normal or markedly subnormal Alkaline Phosphatase (<40 IU/L).

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#### Factors Associated with Low Platelet Count in Veterans with Chronic Hepatitis C

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**Purpose:** The purpose of this study was to examine liver histology and virological characteristics as it relates to HCV-associated thrombocytopenia in a veteran population.

**Methods:** We conducted a retrospective review of patients with chronic HCV who had undergone liver biopsy at the Atlanta Veterans Affairs Medical Center from Jan 1, 1995 to Jan 1, 2006. Data collected included: gender, age, race, laboratory results (ALT, AST, platelet count, HCV genotype, viral load), and histology based on the Scheuer histologic scoring system. We defined low platelet count as  $<150 \times 10^3/\text{mL}$ . Means and categorical variables were compared using ttest and chi square respectively. We used univariate logistic regression to explore the relationship platelet count and various variables. Forward stepwise logistic regression was used to select variables for the final model

**Results:** Information was available for 314 patients. 97% were male and median age was 51 years (range 30–68 years). Median aspartate transaminases (AST) level was 54 IU/L and platelet count was  $213 \times 10^3/\text{mL}$ . 16% of patients had platelet counts  $<150 \times 10^3/\text{mL}$ . On liver biopsy, a majority of the patients had grade 1 and 2 lobular and portal inflammation (33% and 47% for lobular, 47% and 37% for portal respectively) and stage 1 and 2 fibrosis (32% and 25% respectively). A majority of patients were genotype 1 (89%) and 52% had viral loads  $>850,000$  IU/mL. Steatosis was reported in 41% of biopsies. In univariate logistic regression, low platelet count was associated with higher grade of portal (OR 1.9; 95% CI 1.2, 2.8;  $P$ -value 0.001) and lobular (OR 1.7; 1.2, 95% CI 2.6;  $P$ -value 0.004) inflammation, higher stage of fibrosis (OR 1.91; 95% CI 1.4, 2.4;  $P$ -value <0.001) and higher odds of abnormal AST ( $>35$  IU/L) (OR 2.5; 95% CI 1.03, 6.2;  $P$ -value 0.04). No significant relationship was found between low platelet count and viral load, genotype, or steatosis. In multivariable regression analysis, controlling for age, gender, and grade of inflammation, low platelet count was significantly associated with higher stage of fibrosis. The odds of having low platelet count for those with advanced stage of fibrosis (Stage 3–4) were nearly 5.5 times the odds of someone with early fibrosis (stage 0–2) (OR 5.5; 95% CI 2.8, 10.1;  $P$ -value <0.001).

**Conclusion:** Our study did not find genotype, viral load, or steatosis to be predictive of thrombocytopenia in veterans with HCV; however, we did demonstrate a strong association between thrombocytopenia and advanced fibrosis.

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#### Acute Cholecystitis after Percutaneous Liver Biopsy in the Absence of Hemobilia

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**Purpose:** Percutaneous liver biopsy (PCNB) is the standard method for obtaining liver tissue in the management of acute and chronic liver disease. Known complications of PCNB include hemoperitoneum, subcapsular

hematoma, hypotension, pneumothorax and sepsis. Acute cholecystitis associated with hemobilia is very rare and is thought to be secondary to obstruction of the cystic duct by clotted blood. Herein, we describe a unique case of cholecystitis after a PCNB in the absence of hemobilia.

**Case Report:** A 42 year old man underwent an outpatient liver biopsy for staging of chronic hepatitis C. The liver biopsy was uneventful and he was discharged home 4 hours later. The patient presented to the ER that same evening with right upper quadrant pain but was discharged after laboratory studies demonstrated normal liver tests. He returned 48 hours later with worsening right upper quadrant pain associated with nausea and emesis. He was noted to have right upper quadrant tenderness and a positive Murphy's sign. He had a leukocyte count of  $23,000/\text{mm}^3$ , hematocrit of 39%, normal coagulation profile and normal liver tests. Abdominal ultrasound revealed a distended gallbladder with diffuse wall thickening and pericholecystic fluid. There was echogenic material inside. Laparoscopic cholecystectomy was performed the following morning. The gallbladder was distended with moderate amount of blood around the liver and gallbladder. The cystic lymph node was enlarged. On histological examination the gallbladder consisted of moderate amounts of tan-brown viscous fluid and multiple diminutive tan black calculi ranging from 0.1 – 0.3 cm in greatest dimension. The postoperative course was uneventful and the patient was discharged home 2 days later.

**Discussion:** We report an exceedingly rare complication of acute cholecystitis secondary to PCNB. The liver biopsy in our case was performed by a Trucut needle with one pass made. There was a very strong temporal relationship between the procedure and the onset of symptoms, which occurred within 7 hours after the procedure. Although the symptoms and cholecystitis could have been attributable to hemobilia, none was identified at laparoscopy or during pathological assessment after cholecystectomy. We hypothesize that the blood lying around the gallbladder (from the liver biopsy) incited gallbladder wall irritation which then led to acute cholecystitis.

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### Clinical and Histological Differences between Obese and Non-Obese Cryptogenic Cirrhosis

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**Purpose:** Metabolic syndrome of obesity and nonalcoholic fatty liver disease constitutes an important segment of patients with cryptogenic cirrhosis (CC). However, CC is also seen in patients without obesity. The aim of our study was to characterize the clinical, biochemical and histologic differences between obese and non-obese patients with CC.

**Methods:** Thirty two consecutive patients who had liver transplant for CC were categorized into obese ( $\text{BMI} \geq 30 \text{ Kg/M}^2$ ) and non-obese ( $\text{BMI} \leq 25 \text{ Kg/M}^2$ ) groups of 16 cases each. Clinical (Age, gender, concurrent illness, presence of diabetes mellitus) and biochemical parameters (AST, ALT, AST/ALT ratio, alkaline phosphatase /AST ratio) and liver explant histology were compared between the groups. The liver histology was reevaluated by a hepatopathologist for the inflammation, lymphoid aggregate, plasma cells, interface hepatitis, steatosis, perivenular and sinusoidal changes, glycogenated nuclei, Mallory hyaline, bile duct changes, hepatocyte necrosis and fibrosis.

**Results:** *Obese cryptogenic cirrhosis:* The mean age was  $56.6 \pm 8.1$  years, BMI was  $35.0 \pm 3.6 \text{ Kg/M}^2$ , there were more females (75%), concurrent illness was present in 50% and diabetes in 37%. Aminotransferases (AST  $50.1 \pm 23.6 \text{ U/L}$ , ALT  $40.0 \pm 20.7 \text{ U/L}$ ) were mildly increased. On histology steatohepatitis and steatosis were seen in 25% each and in 50% no fatty change was noted. *Non-obese cryptogenic cirrhosis:* The patients were younger ( $48.9 \pm 15.0$  years), BMI was  $22.2 \pm 1.7 \text{ Kg/M}^2$ , there

was no gender difference (female 50%), concurrent illness was present in 43.7% and diabetes in 31%. Aminotransferases (AST  $163.3 \pm 166.3 \text{ U/L}$ , ALT  $110 \pm 106.3 \text{ U/L}$ ) were higher and AST/ALT and alkaline phosphatase/AST ratios were comparable in the two groups. Steatohepatitis was uncommon (6%), steatosis was seen in 44% and 50% did not have fatty change.

**Conclusion:** Non-obese CC as compared to obese CC is characterized by younger age at presentation, absence of gender predilection, higher serum amino-transferases and a very low incidence of steatohepatitis. Steatosis and higher amino-transferases in absence of obesity in some of the CC patients may suggest toxic liver injury to be a causative factor in a subset of non-obese CC.

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### Moexipril in Patients with Non-Alcoholic Fatty Liver Disease

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**Purpose:** The blockade of angiotensin II synthesis attenuates hepatic fibrosis in different experimental models of chronic liver injury. We aimed to determine the safety and efficacy of moexipril, an angiotensin-converting enzyme (ACE) inhibitor, on liver biochemistries in patients with non-alcoholic fatty liver disease (NAFLD).

**Methods:** Four patients with biopsy proven NAFLD were enrolled. Oral moexipril 15 mg/day was administered for 1 year to three patients.

**Results:** No significant changes in serum alkaline phosphatase ( $96 \pm 32$  vs.  $93 \pm 6 \text{ U/L}$ ,  $P = 0.9$ ), total bilirubin ( $1.5 \pm 0.9$  vs.  $2.1 \pm 0.3 \text{ mg/dl}$ ,  $P = 0.7$ ), aspartate aminotransferase ( $48 \pm 9$  vs.  $44 \pm 23 \text{ U/L}$ ,  $P = 0.4$ ), albumin ( $4.4 \pm 0.3$  vs.  $4.2 \pm 0.6 \text{ g/dl}$ ,  $P = 0.9$ ) were noted after 1 year of treatment. One of the 3 patients who received medication withdrew from the study at 6 months. No major adverse reactions were observed, but 2 out of 3 patients complained of increased fatigue.

**Conclusion:** Moexipril was not clinically beneficial to patients with NAFLD.

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### Effect of Diabetes Mellitus on Therapy Discontinuation Rates during Hepatitis C Therapy

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**Purpose:** Hepatitis C is a risk factor for diabetes mellitus (DM). Previous work from our group demonstrated a four times higher risk of DM among our hepatitis C patients. Despite availability of effective therapy for hepatitis C, unacceptably high therapy discontinuation rates remain to be a major barrier to successful therapy outcomes. We evaluated the effect of DM on therapy discontinuation rates of our patients.

**Methods:** A database is established to evaluate the interaction of hepatitis C and DM. We evaluated the treatment patients in this database with emphasis on therapy discontinuation rates.

**Results:** From 1999 – 2006 we had 148 patients in the database treated with interferon based therapies. Mean age was  $53.0 \pm 0.5$ . 98% were male. 51.4% were caucasian, 24.3% were black and 22.3% were hispanic. They included post-transplant, pre-transplant, re-treatment and tx naïve patients. 65.8% were treated with pegylated interferon/ribavirin, 23.6% with rebetron, 1.9% with consensus interferon/ribavirin and 0.6% with pegylated interferon monotherapy. 64 patients (43%) completed therapy. 52 (35.1%) were discontinued for non-response. 32 (21.6%) were discontinued prematurely

secondary to side-effects. In a logistic regression model, using a stepwise approach, after adjusting for age, gender and race, diabetes did not effect the rate of discontinuation among hepatitis C patients with an odds ratio of .066–95% CI (0.28–1.6,  $P$  0.36).

**Conclusion:** Diabetes Mellitus that is highly prevalent in our Hepatitis C patient population did not have significant impact on therapy discontinuation rates.

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### Serum Adipokine Profile in Indian Men with Nonalcoholic Steatohepatitis: Serum Adiponectin Is Paradoxically Decreased in Lean Versus Obese

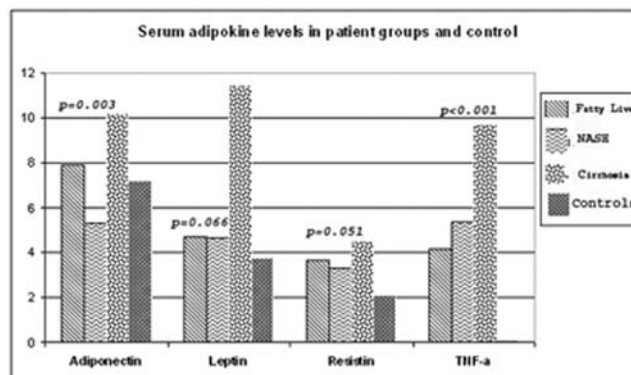
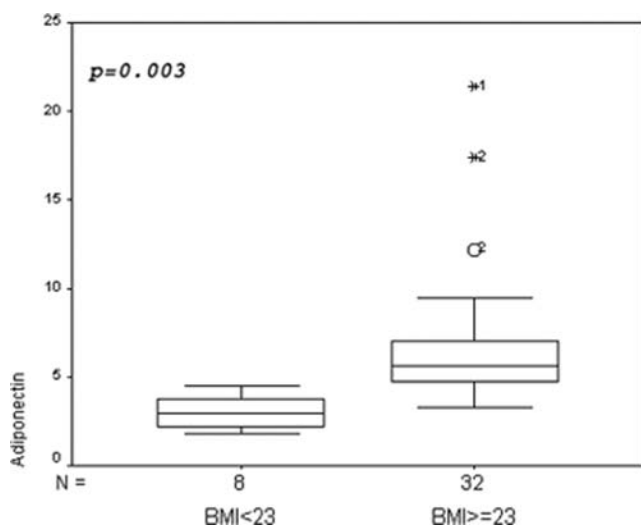
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**Purpose:** Asian Indians are prone to central obesity and for same degree of weight gain are more insulin resistant compared to the West. Hence there is a need to study adipokine profile in nonalcoholic fatty liver disease (NAFLD) and cryptogenic cirrhosis which are associated with Metabolic Syndrome.

**Methods:** Body mass indices, insulin resistance and serum adipokine levels were studied in 56 patients; 10 with fatty liver, 30 with non-alcoholic steatohepatitis (NASH) and 16 with cryptogenic cirrhosis. Eighteen healthy controls were also included.

**Results:** The patients were markedly obese than controls (patients-mean BMI  $26.9 \pm 4.5$ ; control- $22.6 \pm 2.5$ ,  $P < 0.0001$ ). In NASH there was a small but significant decrease in adiponectin level compared to the controls (NASH  $5.4 \text{ mg/ml} \pm 3$ , controls  $7.2 \text{ mg/ml} \pm 2.9$ ,  $P = 0.037$ ). Obese NAFLD patients (BMI  $> 23$ ,  $N = 32$ ) were more insulin resistant than lean (BMI  $< 23$ ,  $N = 8$ ) patients (HOMA-IR: over weight: median  $N = 2.8$ , range = 0.8–16.3 and lean- median  $N = 1.05$ , range = 0.51–2.75,  $P = 0.003$ ). Lean NAFLD patients had adiponectin levels lower than over weight patients ( $3 \text{ mg/ml} \pm 1$  in lean and  $6.7 \text{ mg/ml} \pm 3.8$  in obese,  $P = 0.003$  Fig. 1) All adipokines tested were raised in cirrhosis patients compared to NAFLD and controls. Serum resistin was increased in the patient population ( $3.7 \pm 3 \text{ ng/ml}$ ) than the controls ( $2.1 \text{ ng/ml} \pm 1.7$   $P = 0.007$  T test) but the difference was significant even when cirrhosis patients were excluded ( $3.4 \pm 2.7 \text{ ng/ml}$ ,  $P = 0.03$ )

**Conclusion:** We observed a small but significant decrease of serum adiponectin and an increase in serum resistin and leptin in NAFLD patients compared to controls. The plasma adiponectin levels in lean NAFLD were lower than obese NAFLD. This paradoxical decrease of serum adiponectin as well as low insulin resistance in lean NAFLD suggest a different new etiology for this subset.[figure1][figure2]



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### Incidence and Mortality Trends of Liver Cancer among Puerto Ricans, US Hispanics and Non-Hispanic US Population

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**Purpose:** Hepatocellular carcinoma incidence rates vary greatly among different ethnic groups. Most of the information regarding the epidemiology of liver cancer in Hispanics is based on evaluation of databases in which there is negligible representation of island Puerto Ricans. The aim of this study was to assess the trends in the incidence and mortality rates of liver cancer in Puerto Ricans, United States (US) Hispanics and the US general population.

**Methods:** We analyzed the databases of the Puerto Rico (PR) Cancer Registry, the US SEER 11, and the PR and US Vital Statistics for all cases of liver cancer diagnosed in the period 1992–2001. A trend analysis of the age-standardized liver cancer incidence/mortality rates (per 100,000) was performed using the direct method (Standard World Population 1960) from 1992–2001. Annual percent change (APC) was estimated with the Poisson model using as predictor year of diagnosis.

**Results:** During the study period, Puerto Ricans and US Hispanics (US-H) showed the highest incidence and mortality trends for liver cancer. The incidence of liver cancer remained stable for Puerto Ricans (APC = 0.06%) yet rapidly increased in the US general population (APC = 4.0%) and US-H (APC = 3.73%). The incidence of liver cancer is increasing in all groups and sexes, except among Puerto Rican females who showed a decreasing incidence trend (APC = -1.99%). Puerto Ricans had the highest mortality rates from liver cancer for both sexes and across all age groups, despite exhibiting a decreasing trend during the study period (APC = -1.68). An increasing mortality trend was evident for both US (APC = 1.08) and US-H (APC = 1.14).

**Conclusion:** Both US Hispanics and Puerto Ricans are disproportionately affected by liver cancer having a higher incidence and mortality rates, respectively, in comparison to the US general population. Further studies should explore the reasons for these ethnic disparities.

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### Can Indoleamine 2,3-Dioxygenase Expression in Liver Biopsy Samples from Hepatitis C Infected Patients Predict Response to Treatment? A Subgroup Analysis Comparing African-American vs. Non-African-American Patients

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Georgia, Augusta, GA; Dept. of Pathology, Veterans Affairs Medical Center, Augusta, GA and Immunotherapy Center, Medical College of Georgia, Augusta, GA.

**Purpose:** African-Americans (AA) respond poorly to hepatitis C virus (HCV) treatment compared to the general population. Indoleamine 2,3-dioxygenase (IDO), which is induced by interferon-alpha, has been shown to suppress T-cell proliferation and has been associated with poor response to HCV treatment in a prior study. We hypothesize that the poor response seen in AA group may be related to a difference in hepatic IDO expression.

**Methods:** Immunohistochemical staining for IDO was performed on 107 liver biopsy specimens, obtained prior to treatment, from patients with HCV. Tissue samples were prepared and incubated with a polyclonal rabbit anti-human IDO antibody, and then sequentially incubated with a biotinylated anti-rabbit antibody. Biopsies from HCV-negative transplant donor candidates were used as negative controls. Tumor draining lymph nodes with IDO+cells were used as positive controls. Both AA and non-African-American (non-AA) groups received pegylated interferon and ribavirin for HCV treatment for at least 48 weeks with sustained virologic response (SVR) defined as viral load undetectable for at least 6 months after end of treatment. *P* values were generated using chi-square analysis.

**Results:** Ethnic cohorts were classified as AA and non-AA subgroups. There was no significant difference in co-morbidities and HCV genotype between the two groups. Among non-AA, IDO expression in responders and non-responders did not significantly predict response to HCV treatment (81% and 92% respectively, *P* = 0.39). Among AA, IDO expression in responders was greater than non-responders, however, this did not meet statistical significance (31% and 0% respectively, *P* = 0.27).

**Conclusion:** IDO expression was associated with HCV treatment non-responders in a prior study, however, results were not stratified according to race. In our study, there was a trend towards greater IDO expression among responders in the AA group (not statistical significant). Hepatic IDO staining may serve as a predictor of HCV treatment success in AA subgroups, however, larger studies will be needed to confirm this.

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#### Effects of Pentoxifylline and Weight Reduction on Liver Histology in Patients with Non-Alcoholic Steatohepatitis (NASH)

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**Purpose:** We studied the effects of 6-months of pentoxifylline (TNF- $\alpha$  antagonist) therapy on liver histology in patients with NASH.

**Methods:** Patients of NASH, serum ALT  $>1.2 \times$  ULN for  $>6$  mo were enrolled. Excluded: alcohol  $>20$  g/wk, viral/autoimmune hepatitis, PBC,

biliary obstruction, Wilson disease, haemochromatosis, cirrhosis, and drugs. Patients received pentoxifylline, 400 mg tid  $\times$  6 mo with weight reduction. Repeat liver biopsy was done after 6 mo. Brunt's grade and fibrosis were compared pre- and post-therapy. Histological response: at least one grade reduction in Brunt's grade from the baseline.

**Results:** 15 patients were included (age  $33.1 \pm 7.4$  yrs, M:F 13:2). Baseline biopsy: steatosis (grade I in 3, grade II in 4, grade III in 8), lobular inflammation (grade 0 in 1, grade 1 in 3, grade 3 in 11), portal inflammation (grade 0 in 3, grade 1 in 12), and fibrosis (grade 1 in 13, grade 2 in 2). Brunt score was grade 1 in 3, grade 2 in 6 and grade 3 in 6 patients. Post-therapy Brunt's grade decreased by at least one grade (responder) in 8 (53%). Portal inflammation and fibrosis did not decrease even in responders.

**Conclusion:** Pentoxifylline improves or stabilizes the markers of acute injury in liver histology like steatosis, and lobular inflammation. Longer periods of therapy and/or higher dosages may be required for reversal of fibrosis in these patients.

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#### The Value of Serum Aminotransferases after Cardio-Pulmonary Resuscitation

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**Purpose:** Liver function tests are commonly done after cardio-pulmonary resuscitation (CPR). However the clinical value of these measurements in predicting mortality is unclear and never studied before.

**Methods:** A retrospective review of medical records of patients  $\geq 18$  years who underwent CPR or were evaluated for clinical instability with anticipated cardio-pulmonary arrest at our hospital over a period of one year was performed. We obtained baseline and post event serum aminotransferases. Exclusion criteria were unavailability of baseline or post event serum aminotransferases or if patients did not survive initial resuscitation. Patients were divided into 2 groups: discharged alive (group A) and died during hospitalization (group B).

**Results:** Sixty patients fulfilled study criteria. The median age was 66 years and there were 31 men and 29 women. The predominant primary diagnosis was sepsis (72%, 43/60). Among 23 patients with underlying liver disease, 11 had chronic hepatitis, 2 had fatty liver and 10 had other liver pathology. Thirty percent (18/60) had cardio-pulmonary arrest and 70% (42/60) had clinical instability with anticipated arrest. Forty-eight patients (80%, 48/60) had baseline aminotransferases  $\leq$  upper limit of normal (ULN; 38 IU/mL) and 3 (4%, 3/60) had baseline aminotransferases more than twice ULN. There were 34 patients in Group A and 26 patients in Group B. In Group A mean change in AST was 9 IU/mL and mean change in ALT was 12 IU/mL. In Group B mean change in AST was 743 IU/mL and mean change in ALT was 359 IU/mL. In further calculation, six patients with extreme changes in

Parameters	Responders (N = 8)			Non-responders (N = 7)		
	Baseline	Post-therapy	<i>P</i> value	Baseline	Post-therapy	<i>P</i> value
Brunt's grade	2.6 $\pm$ 0.5	1.4 $\pm$ 0.5	$<0.01$	1.7 $\pm$ 0.7	2.0 $\pm$ 1.0	0.17
Steatosis	2.9 $\pm$ 0.4	1.2 $\pm$ 0.7	$<0.01$	1.7 $\pm$ 0.8	1.8 $\pm$ 0.9	0.6
Ballooning	1.2 $\pm$ 0.7	0.6 $\pm$ 0.5	0.01	1.4 $\pm$ 0.5	1.4 $\pm$ 0.8	1.0
Lobular inflammation	1.9 $\pm$ 0.4	1.1 $\pm$ 0.4	$<0.01$	1.4 $\pm$ 0.8	1.4 $\pm$ 0.8	1.0
Portal inflammation	0.9 $\pm$ 0.4	0.9 $\pm$ 0.4	1.0	0.7 $\pm$ 0.5	1.0 $\pm$ 0.6	0.17
Fibrosis	1.2 $\pm$ 0.5	1.5 $\pm$ 0.8	0.35	1.0 $\pm$ 0.8	1.3 $\pm$ 0.8	0.36
BMI	23.9 $\pm$ 3.4	21.3 $\pm$ 2.4	$<0.01$	24.2 $\pm$ 1.8	23.3 $\pm$ 2.2	0.2
AST	77.0 $\pm$ 25.5	34.7 $\pm$ 16.5	0.02	73.0 $\pm$ 24.4	30.9 $\pm$ 13.1	$<0.01$
ALT	118.7 $\pm$ 55.2	34.2 $\pm$ 8.3	$<0.01$	115.1 $\pm$ 46.2	53.1 $\pm$ 41.2	$<0.01$
HOMA	3.8 $\pm$ 1.96	1.6 $\pm$ 0.6	0.02	2.6 $\pm$ 0.7	2.0 $\pm$ 1.2	0.1
TNF- $\alpha$	40.5 $\pm$ 43.6	8.2 $\pm$ 1.4	0.47	13.3 $\pm$ 8.0	16.8 $\pm$ 17.2	0.78

aminotranferases (all belonged to group B) were excluded. Among the 20 patients included in Group B, mean change in AST was 42 and mean change in ALT was 23. Absolute change in AST was significantly higher in Group B than group A ( $P = 0.019$ ). Though there was a higher absolute change in ALT in Group B it did not reach statistical significance ( $P = 0.39$ ). Among patients who developed cardiac arrest, HIV patients were 4 times more likely and chronic hepatitis patients were 8 times more likely to develop ischemic hepatitis.

**Conclusion:** As per our review, an increase in AST level after a cardio-pulmonary resuscitation is associated with higher in-hospital mortality. These results need to be verified in a larger group of patients. Our study is the first to report the association between change in serum aminotranferases and in-hospital mortality after CPR.

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### Systemic and Pulmonary Hemodynamics in Patients with Extra-Hepatic Portal Vein Obstruction (EHPVO)

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**Purpose:** Extra-hepatic portal vein obstruction (EHPVO) is a common cause of portal hypertension and variceal bleeding. Few studies have been done on hemodynamic alterations in patients with non-cirrhotic portal hypertension especially EHPVO in contrast to many reports on hemodynamics in cirrhotics. We evaluated alterations of systemic and pulmonary vascular system in patients with EHPVO and compared them with patients with compensated cirrhosis. The rationale for this investigation was to study the role of portal hypertension *per se* on systemic and pulmonary hemodynamics in EHPVO as compared to the hemodynamic changes produced by hepatic dysfunction *plus* portal hypertension in cirrhotics.

**Methods:** Consecutive patients of EHPVO,  $\geq 15$  years of age were included. Controls were consecutive patients with compensated cirrhosis and history of variceal bleed, matched for variceal status (to ensure that they had same degree of portal hypertension) and body surface area, attending our department during the same period. The hemodynamic studies were HVPG, right atrial pressure (RAP), pulmonary arterial pressure (PAP), pulmonary capillary wedge pressure (PCWP) and mean arterial pressure (MAP). Cardiac output (CO), systemic vascular resistance and pulmonary vascular resistance were calculated.

**Results:** The baseline parameters in the two groups were comparable. Both EHPVO patients and cirrhotics had similar values in all the measured hemodynamic parameters. The mean cardiac output in EHPVO was  $6.5 (\pm 2.6)$  L/min while it was  $7.9 (\pm 3.2)$  L/min in cirrhosis ( $P = 0.212$ ). The systemic vascular resistance in EHPVO was  $1242 (\pm 494)$  dyn.s.cm<sup>-5</sup>, which was similar to that in cirrhotics ( $1018 \pm 355$ ,  $P = 0.167$ ). Similarly the values of pulmonary vascular resistance were comparable in the two groups ( $68 [\pm 60]$  vs.  $71 [\pm 70]$ ,  $P = 0.905$ ). A subgroup analysis was done of 8 patients of EHPVO and 8 age matched compensated cirrhotics which also revealed similar cardiac index, cardiac output, systemic vascular resistance index, systemic vascular resistance, pulmonary vascular resistance index, and pulmonary vascular resistance in the two groups.

**Conclusion:** EHPVO has features of hyperdynamic circulation, ie increased cardiac output, decreased systemic and pulmonary vascular resistance. These changes are similar to that seen in patients with cirrhosis. This suggests a predominant role of increased resistance and thus increased porto-systemic collateral circulation *per se* rather than hepatocellular injury in the genesis of these hemodynamic alterations.

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### MyD88-Dependent Bone Marrow-Derived Cells Mediate Sensitization to Lipopolysaccharide-Induced Acute Liver Injury

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**Purpose:** Toll-like receptors (TLRs) expressed on both immune cells and hepatocytes in the liver recognize microbial danger signals and regulate immune responses. TLR9 and TLR2 play a role in *Propionibacterium acnes* (*P. acnes*)-induced sensitization to lipopolysaccharide (LPS)-triggered acute liver failure (ALF). Both TLR9 and 2 are dependent on the intracellular adaptor, Myeloid Differentiation primary response gene 88 (MyD88).

**Aim:** To determine the differential contribution of immune and parenchymal liver cells in TLR9 + 2-mediated sensitization to LPS-induced ALF and assess MyD88 utilization.

**Methods:** Chimeras were generated in wild type (WT) and MyD88-deficient mice with WT bone marrow (BM) (referred to as WT/WT and MyD88<sup>-/-</sup>/WT, respectively), or in WT mice with MyD88-deficient BM (WT/MyD88<sup>-/-</sup>). Mice of WT, MyD88-deficient and the above chimeric genetic background were primed with TLR9 [ $2.5\mu\text{g/g}$  body weight (BW) intraperitoneal injection (i.p.)] plus TLR2 (LTA  $5\mu\text{g/g}$  BW i.p.) ligands, heat-killed *P. acnes* (positive control; 1 mg i.p.) or saline (negative control) followed 3–7 days later by an LPS challenge ( $0.5\mu\text{g/g}$  BW i.p.).

**Results:** Selective priming with TLR9 + 2 ligands or with *P. acnes* resulted in liver granulomas and significant elevations in serum ALT and LPS-induced serum cytokine levels, namely tumor necrosis factor alpha (TNF $\alpha$ ), interleukin 6 (IL-6), IL-12, and interferon gamma (IFN $\gamma$ ), in WT, WT/WT, and in MyD88<sup>-/-</sup>/WT mice compared to LPS stimulation alone without prior priming. In contrast, MyD88-deficient or WT mice with MyD88-deficient BM-derived cells (WT/MyD88<sup>-/-</sup>) were protected from TLR9 + 2 ligand- or *P. acnes*-induced granulomas, increase in ALT or sensitization to LPS-induced elevation of TNF $\alpha$  or IFN $\gamma$ ; low levels of IL-12 and IL-6 were induced by LPS. Thus, in the MyD88-deficient and WT/MyD88<sup>-/-</sup> mice, priming with TLR9 + 2 ligands or *P. acnes* did not induce any sensitization to LPS-mediated ALF.

**Conclusion:** Bone marrow-derived immune cells play a critical role in TLR-mediated sensitization and induction of ALF. Thus, MyD88-mediated pathways represent a potential target for therapeutic interventions in ALF.

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### Long Term Sustained Virological Response among Hispanic Veterans Successfully Treated for Hepatitis C Virus

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**Purpose:** Few studies have documented the long term durability of sustained virological response (SVR) after chronic hepatitis C virus (HCV) treatment and the optimal follow up for these patients is still not clear. Current studies have documented relapse rates between 0–5%, but none of these were aimed at an Hispanic population. Our goal was to assess the long term virological and biochemical outcome in Hispanic veterans who have documented SVR after interferon-based therapy.

**Methods:** Patients with documented SVR after receiving treatment with standard interferon (IFN) or pegylated interferon (PEG) based regimens, between 1990 and 2005 were invited to participate. Study consisted of a one time visit where a questionnaire was administered to evaluate for recent risk factors for HCV re-infection and blood samples were drawn for AST, ALT and viral load. Statistical analysis was done using Pearson Chi-Square using SPSS software.

**Results:** The study group consisted of 63 patients, 62 males and 1 female with a mean age of 54.1 years (range 37–70). The average follow up time after end of treatment was  $36.24 \pm 13.13$  months (range 15–77). 35 (55.6%) patients had genotype 1, 17 (27.0%) genotype 2, 2 (3.2%) genotype 3 and 1 (1.6%) genotype 4. In 8 (12.7%) patients the genotype was not available. There was no statistical difference in long term SVR between genotypes. 31 (49.2%) patients received IFN and ribavirin, 28 (44.4%) PEG and ribavirin and 4 (6.3%) IFN monotherapy. There was no difference in long term SVR among these 3 groups. Elevation of AST was seen in only 5 (7.9%)

patients. ALT at the time of analysis was normal in all. None [0/58 (0%)] of the patients who presented with normal enzymes had detectable viral load, whereas 20% (1/5) of those with altered liver function tests had evidence of viremia ( $P < 0.001$ ). Overall, only 1 (1.6%) patient of our study group had evidence of virological relapse, which was documented 30 months after the end of therapy. No risk factors for re-infection were identified by the study questionnaire.

**Conclusion:** This study demonstrates that in our Hispanic patients there is a low relapse rate after SVR is achieved, regardless of treatment or HCV genotype. The durability of the SVR in our population is similar to that reported for other ethnic groups. This study supports the evidence that routine follow up viral loads after SVR has been documented are of low yield, and probably indicated only in patients with altered liver function tests.

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### Large Volume Paracentesis Can Be Performed Safely by a Nurse Practitioner and Can Reduce Physician Work-Load in a Busy GI Practice

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**Purpose:** Due to time constraints, fewer physicians are performing LVP resulting in a longer waiting time and more ER and hospital admissions. At our institution, after initial supervision, a certified nurse practitioner (NP) has independently performed LVP in a dedicated cirrhosis clinic. The purpose of our study was to evaluate the feasibility and safety of LVP performed by a NP.

**Methods:** Retrospective review of patients records undergoing LVP between Jan 2003 and May 2007. Baseline information included age, gender, race, etiology of cirrhosis, child's score, and biochemical profile obtained closest to LVP. Information on the practitioner performing LVP (physician or NP), number of attempts, and volume of fluid removed were recorded. Complications including circulatory dysfunction, bleeding, local leakage of ascitic fluid, infection, perforation, and death were compared between the two groups.

**Results:** Baseline characteristics of patients undergoing LVP were similar in two groups as shown in Table 1.

Baseline Characteristics of Patients Undergoing LVP

	Nurse Practitioner	Physician
Number of patients	41	43
Age (yr, range)	66(44–82)	60(44–81)
Gender (M/F)	41/0	43/0
Etiology of liver disease		
Hepatitis C	4 (10%)	4 (9%)
Alcohol	19 (46%)	22 (51%)
Hepatitis C and alcohol	15 (37%)	12 (28%)
Hepatitis B	2 (5%)	1 (2.5%)
Cryptogenic	0	3 (7%)
Hemochromatosis	1 (2%)	1 (2.5%)
Childs Pugh Class		
B	5 (12%)	6 (14%)
C	36 (88%)	37 (86%)

In terms of complications, there was no statistical difference whether LVP was performed by a physician or a NP as shown below.

**Conclusion:** Our study shows no difference between physician and NP performance of LVP and complication rates. We found that LVP performed by a NP is feasible and has acceptable rate of complications. The cost-effectiveness of this model needs to be evaluated.

LVP Results and Complications

	Nurse Practitioner	Physician
Number of paracentesis	245	244
Volume of ascites removed	7796	7004
Number of Needle Attempts	1.06	1.14
Complications (NS)	15 (6.1%)	15 (6%)
Post Paracentesis Circulatory Dysfunction (NS)	6 (4%)	3 (1.2%)
Leakage at site (NS)	4 (1.6%)	4 (1.6%)
Bleeding (NS)	3 (1.2%)	5 (2%)
Infection (NS)	2 (0.8%)	3 (1.2%)
Death	0	0

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### Anticoagulation Therapy Using with Danaparoid Sodium for Portal Venous Thrombosis

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**Purpose:** It is reported that portal venous thrombosis is caused concomitantly with a variety of diseases. However, the adequate treatment for portal venous thrombosis has yet to be established. In this study, we examined the effect of anticoagulation therapy using with danaparoid sodium for portal venous thrombosis.

**Methods:** Portal venous thrombosis has been confirmed in 22 out of 641 cases of liver cirrhosis in our hospital since 1995. Danaparoid sodium is a low molecular weight heparinoid whose major component is heparan sulfate. Danaparoid sodium enhances the effect of antithrombin that inhibits coagulation factor. Compared to heparin and low molecular weight heparin, danaparoid sodium has a higher selective anti-Xa factor activity with lower risks of hemorrhage. Danaparoid sodium was administered to seven patients with portal venous thrombosis who were considered to have developed new thrombosis. One ampule (1250 anti Xa factor units) of danaparoid sodium was slowly injected intravenously every 12 hours (twice a day). After administration of danaparoid sodium, follow-ups by abdominal ultrasonography and CT were performed every two weeks. We studied the effects of danaparoid sodium by examining clinical findings, laboratory data, and imaging findings.

**Results:** In all seven patients who were administered danaparoid sodium, patients were safely treated without any adverse effects and complications. Thrombosis in five out of seven patients disappeared within four weeks. However, recurrence of thrombosis was found after discontinuation of administration of danaparoid sodium in three out of five cases. In order to prevent recurrence, maintenance therapy by warfarin and aspirin was implemented after discontinuation of danaparoid sodium for some patients. However, it was not effective. When danaparoid sodium was re-administered to the recurrence cases, thrombosis disappeared within four weeks in all three recurrent cases. No adverse effect was found when danaparoid sodium was re-administered.

**Conclusion:** It was suggested that danaparoid sodium might become an effective drug for treatment of portal venous thrombosis, since it was effective easily administered, and unlikely to cause adverse effects such as hemorrhage. We intend to examine indications, administration method, and establishment of maintenance therapy by investigating more cases.

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### Efficacy of Recombinant Hepatitis B Vaccine (rHBV) Alone in Preventing Perinatal Transmission of Hepatitis B Is Similar to

### Combination of rHBV Plus Hepatitis B Immunoglobulin (HBIG): A Randomized Controlled Trial

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**Purpose:** HBIG is given along with rHBV to neonates born to HBsAg-positive mothers to prevent perinatal transmission of Hepatitis B (HBV). However HBIG is costly and not widely available. We compared the protective efficacy of combination of HBIG plus rHBV versus rHBV alone for prevention of perinatal transmission of HBV.

**Methods:** Neonates delivered of consecutive HBsAg positive mothers received either HBIG (0.5 ml) plus rHBV (Group-A) or rHBV alone (Group-B). rHBV vaccination schedule was 0, 6, 10, and 14 weeks of age in both the groups and anti-HBs titers were determined at weeks 6 and 18. Development of anti-HBs >10 IU/ml at any time was considered protective. HBsAg and HBV DNA were also determined at 18 wks.

**Results:** 79 HBsAg positive full-term mothers were included (17 [22%] HBeAg positive, 50 [63%] with serum HBV-DNA >5 pg/ml). 40 neonates were randomized to Group-A and 39 to Group-B. At 6 wks, protective anti-HBs titers developed more in Group-A than Group-B (21/28 [75%] vs 7/25 [28%],  $P = 0.001$ ). However, by 18 wks, protective anti-HBs titers were similar in both the groups (30/31 [97%] vs 26/29 [90%];  $P = 0.35$ ). Protection could not be determined in 19/79 infants (3 died, 16 follow-up awaited). At 18 wks 4/53 (8%) had positive HBsAg and HBV-DNA suggestive of intrauterine transmission. Protection was similar in both groups regardless of mothers' HBeAg status and maternal HBV-DNA level.

**Conclusion:** rHBV alone and rHBV plus HBIG give similar protection against hepatitis B by 18 wks of age, irrespective of maternal HBeAg status or HBV-DNA positivity. At 6 wks, combination of rHBV plus HBIG offers better protection than rHBV alone.

Parameter	Baseline	6 Weeks	18 Weeks
Protective (>10 IU/ml) Anti-HBs			
Group A	—	21/28 (75%)	30/31 (97%)
Group B	—	7/25 (28%) ( $P = 0.001$ )	26/29 (90%) ( $P = NS$ )
HBsAg			
Group A	18/39 (46%)	0/27 (0%)	1/26 (4%)
Group B	17/38 (45%)	0/26 (0%) ( $P = NS$ )	3/27 (11%) ( $P = NS$ )
Detectable HBV DNA			
Group A	19/32 (59%)	10/27 (37%)	16/26 (62%)
Group B	21/30 (70%)	12/26 (46%) ( $P = NS$ )	11/27 (41%) ( $P = NS$ )
HBeAg			
Group A	4/38 (10%)	—	1/25 (4%)
Group B	2/30 (7%)	—	2/25 (8%) ( $P = NS$ )
Any marker of HBV present (HBsAg, HBeAg, HBV DNA)			
Group A	25/39 (64%)	10/27 (37%)	17/25 (68%)
Group B	27/38 (71%)	12/26 (46%) ( $P = NS$ )	11/25 (44%) ( $P = NS$ )

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### Treatment Outcomes of Transcatheter Arterial Chemoinfusion (TACI) in Patients with Unresectable Hepatocellular Carcinoma (HCC) Prior to Orthotopic Liver Transplantation

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**Purpose:** Transcatheter arterial chemoembolization (TACE) is a common therapy for unresectable HCC. While both TACE and TACI are generally well tolerated by patients with compensated liver disease, those with poor hepatic tend to have higher rates of complications. Compared to TACE, TACI without embolization may have similar efficacy with fewer side effects and

may allow us to include patients with less hepatic reserve. Our purpose is to examine outcome of TACI in HCC patients awaiting orthotopic liver transplantation (OLT) and its efficacy as a bridge towards transplantation.

**Methods:** We performed a retrospective study of 160 TACI cases in 82 HCC patients between 4/98–3/07 at single U.S. medical center. We examined 30 and 90 day- morbidity following TACI. We also measured overall patient mortality while waiting on transplantation list.

**Results:** Mean age was  $55 \pm 7$ , 84% were male, 44% were Asian and 41% were white. Most had cirrhosis (88.6%), and either chronic hepatitis C (62.0%) or B (32.9%). TNM staging of I, II, III and IV were 25%, 57%, 13% and 5%, respectively. Mean MELD score was  $10.1 \pm 4.1$  and mean CTP score was  $6.5 \pm 1.7$ . Number of patients with Child A, B, C was 45, 25, 7, respectively. 40 patients underwent OLT. The average waiting period to OLT is 6 months. Among 42 patients on waiting list, 7 patients died. The cause of death for the seven patients include multiorgan failure, metastasis, recurrent hepatitis C and infection. Only one patient died in 90 days following TACI and the other 6 patients died in the one or two years following TACI. Among the remaining 35 patients, 23 patients are alive and remained on transplantation list and 12 patients are lost for follow up. Only 7 patients were hospitalized for >24 hours (6.25% = 10/160 cases) The cause of hospitalization for >24 hours include nausea, vomiting, fever, variceal bleeding and encephalopathy. One patient (0.63% = 1/160 cases) had worsening of liver function at the same day following first TACI procedure.

**Conclusion:** TACI is an effective and safe treatment for unresectable HCC prior to OLT. Most of our patients required less than 24 hours of hospitalization, while patients undergoing TACE generally require longer hospitalization. Rate of worsening of liver function following was only 0.63%. Rate of mortality related to TACI was 1.43% (1/70). TACI may be used as an effective bridge towards transplantation.

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### Factors Associated with Treatment Failure in Patients with Genotype 3 Hepatitis C Virus Infection

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**Purpose:** Patients with hepatitis C virus (HCV) genotype 3 are believed to have better response to therapy and only require 24-week therapy. However recent data showed there is increasing non-response rate up to 20% in these patients. Little is known about the factors associated with their therapy failure.

**Methods:** We conducted retrospective chart review on 34 pts with HCV genotype 3 infection who were treated with Peg-interferon and ribavirin from 2005 to 2006. Patients were excluded if they were not naive to interferon-based therapy, were non-compliant, or lost to follow up. Data were collected on pt demographics (age, sex, and body weight), comorbidities (DM), baseline HCV RNA levels and baseline ALT levels. HCV RNA and ALT levels were repeated at 12 wks and 24 wks of treatment. All pts had follow-up in 6 months post treatment completion to confirm sustained virological response (SVR). Univariate and multivariate regression analyses were performed to identify factors associated with treatment response.

**Results:** Among the 34 patients in our study, 16 (47%) were female. The mean age was  $42.8 \pm 10.5$  years old; the mean body weight was  $80.7 \pm 18.3$  kg; the mean baseline HCV RNA level was  $5.5 \pm 0.8$  log IU/mL; the mean baseline ALT was  $104.6 \pm 79.8$  IU/dL. Eighteen pts achieved SVR, and 16 patients failed to respond to therapy. In a univariate analysis, age was found negatively associated with treatment response (odds ratio [OR] 0.80; 95% CI 0.70–0.92;  $P = 0.002$ ), while sex, body weight, baseline ALT levels, and baseline HCV RNA levels did not have significant association with SVR. In a multivariate analysis adjusting for sex, body weight and baseline ALT levels, age remained negatively associated with treatment response (OR 0.66; 95% CI 0.48–0.92;  $P = 0.01$ ).

**Conclusion:** Therapy response to interferon-based regimen in pts with HCV genotype 3 infection is negatively affected by increasing age, suggesting that elderly pts (>50 years old) with genotype 3 infection may need longer duration of therapy. Further large-scaled studies are needed to confirm these findings and evaluate potential factors associated with treatment response in this patient group.

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#### Improvement of Metabolic Syndrome (MS) in Patients with Non-Alcoholic Fatty Liver Disease (NAFLD) after Bariatric Surgery

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**Purpose:** Non-alcoholic fatty liver disease (NAFLD) and metabolic syndrome (MS) are commonly found in morbidly obese patients undergoing bariatric surgery.

This study aims to assess the impact of weight loss surgery on the clinical outcomes of morbidly obese patients with NAFLD.

**Methods:** 286 morbidly obese patients with biopsy-proven NAFLD who underwent bariatric surgery were included. Clinical, demographic and histologic data were available at the time of surgery and for a follow-up period after surgery. MS was defined according to ATP III (The Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults).

**Results:** Clinical, demographic and laboratory data for the entire cohort are as follows: age  $44.0 \pm 11.5$ , female 78%, BMI  $48.7 \pm 9.4$ , waist circumference  $139 \pm 20$  cm, AST  $23.9 \pm 14.9$ , ALT  $30.0 \pm 20.1$ , diabetes mellitus (DM) 30.1% and MS 39.2%. Patients underwent restrictive, malabsorptive or combination surgical procedures. Of the entire cohort, 27.3% underwent malabsorptive surgery, 55.9% underwent restrictive surgery and 16.8% underwent combination restrictive-malabsorptive surgery. Mean weight loss after restrictive surgery was  $33.7 \pm 20.1$  kg (follow up period  $298 \pm 271$  days). On the other hand, the mean weight loss after malabsorptive surgery was  $39.4 \pm 22.9$  kg (follow-up period  $306 \pm 290$  days) and after combination surgery, the mean weight loss was  $28.3 \pm 14.1$  kg (follow up period  $281 \pm 239$  days). The amount of weight loss post-surgery was not significantly different among the three bariatric surgery procedures ( $P = 0.352$ ). Regardless of the type of bariatric surgery, significant improvements were noted in DM ( $P$ -values from  $<0.0001$  to  $0.0005$ ), MS ( $P$ -values from  $<0.0001$  to  $0.01$ ), waist circumference ( $P$ -values  $<0.0001$ ), BMI ( $P$ -values  $<0.0001$ ), fasting serum triglycerides ( $P$ -value  $<0.0001$  to  $0.001$ ), and fasting serum glucose ( $P < 0.0001$ , except for the combination surgery). Additionally, a significant improvement in ALT/AST ratio ( $P = 0.0002$ ) was noted only in those who underwent restrictive surgery.

**Conclusion:** Weight loss after bariatric surgery is associated with a significant improvement in MS and other metabolic factors associated with NAFLD.

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#### Association of Nonalcoholic Fatty Liver Disease with Metabolic Syndrome in Indian Population

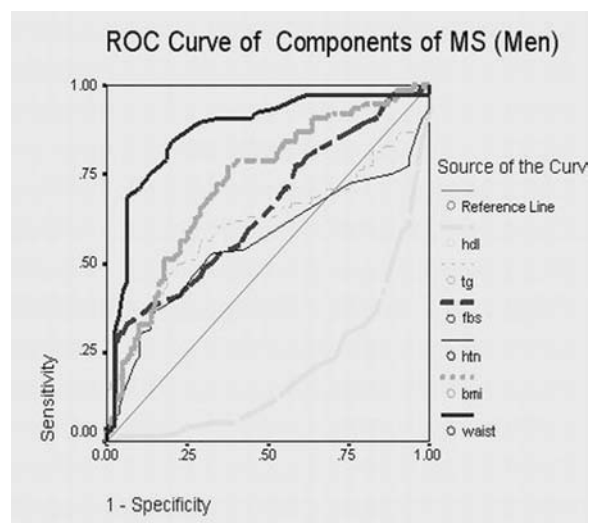
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**Purpose:** Association between non-alcoholic fatty liver disease (NAFLD) and metabolic syndrome varies among populations. There is a need to evaluate this in the Indian subcontinent specially using modified ATP III criteria with waist circumference lowered to 90 and 80 cm in men and women respectively.

**Methods:** 76 asymptomatic patients with fatty liver persistently for an year or more on US abdomen, with or without abnormal LFT and 100 age sex matched healthy controls were studied. The anthropometric measurements, metabolic parameters, LFTs and liver histology were analyzed in all patients.

**Results:** 60 men, mean age  $40.05 \pm 11.4$  years, range 18–66. 63 had NASH and 13 had cirrhosis. 49 (64.5%) patients had raised ALT while 35.5% of the total patients and 25.4% of the biopsy proven NASH patients had normal ALT levels. 21% of the patients compared to 8% controls ( $P < 0.01$ ) had associated MS as per standard and 42.1% and 12% when the revised ATP-III criteria used. ROC curve analysis showed waist circumference had the best power of all ATP-III components in discriminating a patient from control. 35% of nondiabetic patients were insulin resistant with HOMA-IR cutoff set at 3. In patients compared to controls, the mean BMI ( $25.2$  vs.  $22.7$ ,  $P < 0.01$ ) and waist circumferences ( $92.9$  vs.  $80.8$  cm,  $P < 0.01$ ) were higher. 79% of the patients and 44% of the controls were over weight. At presentation Stage 1 fibrosis was seen in 30 (39.5%), stage 2 in 10 (13.2%), stage 3 in 6 (7.9%) and stage 4 in 13 (17.1%) patients. Fibrosis score showed a positive correlation between FBS ( $r = 0.25$ ,  $P = 0.029$ ) and negative correlation between HDL ( $r = -0.33$ ,  $P = 0.004$ ). No significant relation between the number of positive criteria as per ATP-III and the degree of fibrosis ( $r = 0.06$ ,  $P = 0.61$ ) was found.

**Conclusion:** ALT values could be deceptive in a significant proportion of Indian NAFLD. Significant proportion are asymptomatic and present at late stages. While insulin resistance and obesity are common, waist circumference is the most dominant determinant of NAFLD. The association of NAFLD with MS is not strong enough. This study also shows that in a proportion of patients, NAFLD develops in the absence of evidence of MS.[figure 1]



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#### Sustained Virological Response to Interferon-Based Antiviral Therapy by Viral Genotype in Recurrent Hepatitis C Patients Following Liver Transplantation

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**Purpose:** We conducted a retrospective review of sustained virological response (SVR) rates to interferon-based antiviral therapy by viral genotype at our institution in posttransplant patients with recurrent hepatitis C virus (HCV) infection.



**Methods:** We identified 224 patients who underwent liver transplantation at our institution for end-stage liver disease for chronic hepatitis C between February 1995 and June 2007. Interferon-based antiviral therapy was instituted in 59 out of 224 with histological evidence posttransplant recurrent HCV. These patients were treated with pegylated interferon and ribavirin. Currently, 4 out of 59 patients are undergoing antiviral therapy and were excluded from our analysis. Data for HCV genotype and SVR were available for 41 (75%) patients.

**Results:** SVR was achieved in 16 (39%) patients, and SVR ranged from 0 to 62.5% by genotype. 9 patients (56%) had genotype 1, 14 patients (87%) were women, and 2 (13%) had diabetes. Average BMI was 29.3 and pre-treatment viral load was  $4.9 \times 10^6$  IU/ml. The odds ratio by genotype 1, female gender, and diabetes was 0.41, 0.71, and 2.72, respectively.

**Conclusion:** Patients with genotype 1 and diabetes were less likely to achieve SVR, whereas female patients more likely to achieve SVR.

SVR By Viral Genotype

Genotype	Number of Patients	SVR	No SVR
1	28	9 (32%)	19 (68%)
2	4	2 (50%)	2 (50%)
3	8	5 (62.5%)	3 (37.5%)
4	1	0 (0%)	1 (100%)

Patient Demographics By SVR

	SVR	No SVR
Number Of Patients	16	25
Genotype 1 (%)	56%	76%
Female (%)	87%	72%
BMI (kg/m <sup>2</sup> )	29.3	26.4
Diabetes (%)	13%	17%
Pre-treatment Viral Load (IU/ml)	$4.9 \times 10^6$	$3.5 \times 10^6$

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### Single Dose of Infliximab Is Safe and Effective in Severe Alcoholic Hepatitis: An Open Label Study

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**Purpose:** Severe alcoholic hepatitis (AH) is associated with high mortality. Tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) contributes to the progression of AH and TNF- $\alpha$  antagonists like infliximab may help in ameliorating the severity and complications of AH. There is contradictory data about the efficacy of infliximab in AH. We evaluated the efficacy of infliximab in improving the severity and one month mortality in patients with severe AH.

**Methods:** Consecutive patients with severe AH (Maddrey's score  $>32$ ) with or without hepatic encephalopathy (HE) were included. Patients with serum creatinine  $>1.5$  mg/dl, severe cardiovascular or cerebrovascular disease, septicemia, active GI bleed, tuberculosis, malignancy, corticosteroids therapy, HBV, HCV or HIV positive were excluded. Infliximab was given in a dose of 5 mg/kg IV at day 0. Conservative therapy including, plasma, albumin, antibiotics and management of encephalopathy were continued. Maddrey's score, peripheral leucocyte count, serum TNF- $\alpha$  levels, C-reactive protein (CRP) and MELD score were measured at baseline and at day 30. All patients abstained from alcohol during the study period.

**Results:** Nineteen patients (mean age  $38.0 \pm 7.0$  yr, all males) fulfilled the selection criteria. Five (26%) patients had HE (grade 1–2), 17 (89%) had esophageal varices and 4 (19%) had baseline DF $>90$ . Infliximab was well tolerated by all the patients. At day 30, compared to baseline, there was significant improvement in median Maddrey's score (66 [range 35–140] vs. 38.4 [range 11.5–182];  $P = 0.003$ ), median peripheral leucocyte count

(6792 [range 5500–10,000] vs. 3000 [range 2090–6000] cells/cumm;  $P = 0.001$ ), median serum TNF- $\alpha$  levels (45 [range 11.2–19880] vs. 20.5 [4–8600] pg/ml;  $P = 0.001$ ), median serum CRP (34 [range 14–67] vs. 12 [range 1–82];  $P = 0.03$ ), and median MELD score (25 [range 17–36] vs. 21 [range 13–36];  $P = 0.001$ ). Two patients (11%) who had H.E developed renal failure and died in the first week. Seventeen patients (89%) were discharged from hospital and survived till day 30. However, over a median follow up of 60 (range 7–150) days, 4 additional patients died; 2 had DF $>90$  and HE at baseline, (2 patients with massive bleed, HE and renal failure, 1 each with tuberculosis and sepsis).

**Conclusion:** In severe AH, single dose infliximab is well tolerated and is associated with significant improvement in indices of severity. However, large randomized controlled trials would be needed before infliximab can be recommended for regular use in AH.

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### Role of Pentoxifylline in PRE-Hepatorenal Syndrome State

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**Purpose:** Hepatorenal syndrome is one of the major complication of chronic liver disease with the very high mortality. Pre-HRS stage (creatinine clearance  $<75$  ml/min and  $>40$  ml/min) is the stage when intervention can prevent development of HRS. Pentoxifylline has been shown in an anecdotal study to prevent HRS in severe alcoholic hepatitis.

**AIM –** To assess the efficacy of pentoxifylline in Pre – HRS.

**Methods:** Chronic Liver Disease patients with Child Pugh score of  $>7$  fulfilling the criteria were included. Patient with HCC, renal failure or active alcohol were excluded. Patient fulfilling the criteria were randomized to receive pentoxifylline 400 mg tid (Gr 1) or placebo (Gr 2) for the six months. Clinical assessment and creatinine clearance was repeated after 6 months.

**Results:** Twelve patients were enrolled with six patients in each group. Mean age of the patients were comparable in both groups (Gr 1,  $44 \pm 12$  yr vs Gr 2,  $43 \pm 13$  yr). S. bilirubin was  $1.9 \pm 0.4$  vs  $1.8 \pm .6$  mg% in Gr 1 & Gr 2 respectively ( $P = ns$ ); S. albumin was  $3.2 \pm .9$  vs  $2.8 \pm 0.4$  mg% in Gr 1 & Gr 2 respectively ( $P = ns$ ); CTP score was  $9 \pm 1.7$  vs  $8.7$  in Gr 1 & Gr 2 respectively ( $P = ns$ ); baseline creatinine clearance was  $57.3 \pm 9.6$  vs  $66 \pm 7$  ml/min in Gr 1 & Gr 2 respectively ( $P = ns$ ). In the Gr 1 the mean creatinine clearance changed from  $57.3 \pm 9.6$  to  $84 \pm 29$  ml/min whereas the Gr 2 the mean creatinine clearance changed from  $66 \pm 7$  to  $62 \pm 17$  ml/min. Mean serum creatinine changed from  $1 \pm 0.2$  mg/dl to  $0.8$  mg/dl in Gr 1 but the serum creatinine worsened from  $0.78 \pm .28$  to  $0.8 \pm .18$  in Gr 2. One patient died in the Gr 1 due to upper gastrointestinal bleed and no patient died in Gr 2.

**Conclusion:** Pentoxifylline improves the creatinine clearance in the patient in the pre-HRS stage.

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### Hepatic Vein Pressure Gradient (HVPG) Is a Predictor of the Degree of Liver Fibrosis (LF) in Patients with Chronic Liver Disease (CLD) Due to Hepatitis B Virus (HBV)

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**Purpose:** Biopsy is considered a gold standard for assessing LF. Sample variability (30–40%), interobserver variability and allowing only step-wise evaluation limit its use. HVPG, a measure of portal hypertension (PHT) correlates with LF in CLD due to HCV. However, correlation between HVPG and Fibrosis (F) stage has not been fully investigated in CLD due to HBV.

**Aim:** To evaluate the utility of HVPg for assessing LF in patients with HBV related CLD.

**Methods:** 61 patients with HBV related CLD that underwent both liver biopsy and hepatic hemodynamic studies were studied

**Results:** Of 61 (Age:  $37.9 \pm 15.9$  yr, M = 51) patients with treatment naïve HBV related CLD, 49(80.3%) had clinically significant PHT (HVPg  $\geq 10$  mmHg), 39(63.9%) had severe PHT (HVPg  $\geq 12$  mmHg), 6(9.8%) had HVPg  $\leq 5$  mmHg and 6(9.8%) had pre-clinical PHT (HVPg  $> 5$  but  $< 10$  mmHg). Distribution of F stages 1/2/3/4 were 17(27.9%)/10(16.4%)/20(32.8%)/14(23%) respectively. Distribution of Child stage A/B/C were 46(75.4%)/15(24.6%)/0 respectively. No patient showed clinical features of clinical decompensation. A positive correlation between HVPg and F score was found across all ranges of HVPgs (Table). F score was significantly higher in patients with an HVPg  $\geq 10$  and  $\geq 12$  mmHg than in patients with an HVPg  $< 10$  [Median (range) = 3.0(1.0–4.0) vs. 1.0(0.0–3.0),  $P < 0.001$ ] and  $< 12$  mmHg [Median (range) = 3.0(1.0–4.0) vs. 1.0(0.0–3.0),  $P = 0.001$ ], respectively. ROC curve of HVPg for the prediction of advanced Fibrosis i.e F  $\geq 3$  had an AUC of 0.906. HVPg  $\geq 12.75$  mmHg had a sensitivity of 79% and specificity of 89% for predicting advanced fibrosis on histology. However, 9(36.0%) of 25 patients with HVPg  $< 12.75$  had F  $\geq 3$  and 11(30.6%) of 36 patients with HVPg  $\geq 12.75$  mmHg did not have F  $\geq 3$  representing factors other than LF contributing to higher HVPg and/or sampling limitations of liver biopsy.

**Conclusion:** HVPg correlates well with the degree of histological LF in patients with HBV related CLD. It can be a good alternative and/or additive parameter to liver biopsy in these patients.

Correlations between HVPg and F scores

Group	Correlation Coefficient	P
All Patients	0.693	<0.001
HVPg $< 10$ mm Hg	0.603	0.029
HVPg $\geq 10$ mm Hg	0.512	<0.001
HVPg $< 12$ mm Hg	0.887	<0.001
HVPg $\geq 12$ mm Hg	0.543	<0.001

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#### Recent Application of AASLD Practice Guidelines and US Algorithm for Treatment of Chronic Hepatitis B

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**Purpose:** The AASLD practice guidelines (“guidelines”) and US algorithm by Keeffe et al (“algorithm”) for treatment of the chronic hepatitis B (CHB) were recently updated. Although the differences have narrowed, the treatment threshold for ALT and HBV DNA levels showed a few differences between the two references. We compared the guidelines and the algorithm with the treatment patterns in patients with CHB at our center.

**Methods:** Charts of all new and follow-up patients with CHB seen consecutively in the GI/Liver clinics at our center between 1/07 and 5/07 were reviewed. The patient demographics and baseline disease characteristics were recorded. Treatment patterns have been reviewed and compared with recommendations of both references. Statistic significance of the results was estimated with chi-square and Fisher Exact analysis.

**Results:** There were 159 patients with 67% male and a mean age of 52.4 years (range 24–82). 67% were of Asian ethnicity. Overall, 102 of 159 patients (64%) have been treated. As shown in the table below, 71 of 83 (86%) patients eligible for therapy based on the ALT and viral load alone per guidelines and 88 of 109 (81%) patients meeting the algorithm’s criteria received CHB treatment. The reasons for the non-treatment despite meeting the treatment criteria included patient refusal,  $<$  stage 2 fibrosis by modified Ishak system, and observation period for the new patients. For the patients with ALT  $< 2 \times$  ULN, the treatment rate was higher in HBeAg- positive patients regardless

of the biopsy status. Among patients recommended for observation, there were 29 and 13 patients in the guidelines and algorithm groups, respectively. The presented difference in patient selection method by the guidelines and by the algorithm appears to be statistically significant ( $P < 0.05$ ).

**Conclusion:** Both the updated AASLD guidelines and the US algorithm by Keeffe et al applied similarly to the current practice of CHB management at our center. The US algorithm covers a broader spectrum of patients for initiating treatment than the AASLD guidelines.

	Treatment Indicated		Biopsy Considered before Treatment (# of Biopsies performed)		Observation Suggested	
	Treated	Not-Treated	Treated	Not-Treated	Treated	Not-Treated
AASLD Guidelines (N = 159)	71 (86%)	12 (14%)	27 (57%)/(10)	20 (43%)/(4)	4 (14%)	25 (86%)
US Algorithm (N = 159)	88 (81%)	21 (19%)	14 (38%)/(9)	23 (62%)/(2)	0 (0%)	13 (100%)

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#### Prediction of Histology in Nonalcoholic Fatty Liver Disease: Do Medications Matter?

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**Purpose:** Various clinical and biochemical variables had been used to predict histology in patients with NAFLD. However, medications used to treat different components of the metabolic syndrome, had not been assessed as potential predictors of histology. Aim: To determine the association of chronic use of these medications with liver histology in patients undergoing a liver biopsy for suspected NAFLD.

**Methods:** Patients who underwent liver biopsy for unexplained elevated liver tests, suspected NAFLD, or cryptogenic cirrhosis over a 3 year period at our institution were identified. All liver biopsies were read by an academic pathologist and categorized as FL, possible NASH, NASH or normal. Medications chronically used by patients prior to the time of biopsy and relevant clinical and laboratory variables were recorded. Association between individual variables and diagnoses were studied using the Chi-square test.

**Results:** 65 patients were identified; 6 (9%) with normal histology, 27 (41.5%) with FL, 27 (41.5%) with possible NASH and 5 (8%) with NASH. Relevant clinical, laboratory, and medications data are summarized in the table. Use of insulin and BMI were the only significant variables associated with NASH. While diabetes, higher triglycerides levels, use of TZD’s, metformin, statins and ace-inhibitors were more frequent in NASH patients, these did not reach statistical significance.

Variable	Characteristics of the study subjects				
	Normal N = 6	Fatty Liver N = 27	Possible NASH N = 27	NASH N = 5	P-value
Age	48 (36–60)	52 (25–70)	46 (23–62)	38 (36–51)	ns
BMI	48 (26–58)	32 (25–50)	41 (25–61)	51 (31–58)	0.005
Diabetes	1 (17%)	9 (33%)	13 (48%)	4 (80%)	ns
Triglycerides	125 (79–258)	175 (67–360)	219 (71–497)	231 (86–274)	ns
ALT	47 (12–104)	51 (13–140)	53 (13–225)	59 (25–104)	ns
Metformin	1/17%	6/22%	9/33%	3/60%	ns
TZDs	1/17%	3/11%	4/15%	2/40%	ns
Insulin	1/17%	1/4%	1/4%	2/40%	0.02
Statins	1/17%	10/37%	6/22%	2/40%	ns
Fibrates	0	4/15%	2/7%	0	ns
ACE-I	2/33%	8/30%	9/33%	3/60%	ns

**Conclusion:** Pharmacotherapy for components of the metabolic syndrome was more frequent in patients with NASH in this study, but only insulin use was significantly associated with NASH.

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### Treatment Rates in Patients with Chronic Hepatitis B after Liver Biopsy

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**Purpose:** Clinical practice concerns and recent updates of AASLD Guidelines ("guidelines") and US algorithm (Keeffe et al., 2006) on treatment of chronic hepatitis B (CHB) ("algorithm") have focused attention on the interpretation of ALT and HBV DNA levels with the utility of liver biopsy in CHB treatment decisions. Specifically, we focused on the use of liver biopsy in patients with high viral load having either ALT 1–2 × ULN or normal ALT. We also assessed the rates of treatment for CHB patients after the liver biopsy at our center.

**Methods:** Charts of 159 patients with CHB seen in our ambulatory clinics between 1/07 and 5/07 have been reviewed. Patient demographics, laboratory, histology and clinical data were recorded.

**Results:** 159 patients were seen (67% males, mean age of 52.4 years, 60% of Asian ethnicity), and 42 (26%) of them had a liver biopsy. A total of 34 (81%) patients were treated either before or after biopsy (see Table). Overall, 35 of 42 (83%) patients had liver biopsy prior to making initial therapeutic decisions, and 27 of the 35 (77%) patients started treatment. Among 47 patients with ALT 1–2 × ULN, 14 (30%) had a liver biopsy, including 6 subjects who had > stage 1 fibrosis on modified Ishak system. Similarly, among 37 patients with normal ALT and HBV DNA > 20,000 IU/mL (HBeAg-positive) or > 2,000 IU/mL (for HBeAg-negative), 11 (30%) had a liver biopsy, including 4 subjects with > stage 1 fibrosis. The majority of liver biopsy was obtained from the group with ALT > 2 × ULN (24 patients). 14 (58%) of those 24 subjects demonstrated > stage 1 fibrosis. The overwhelming reasons for non-treatment were minimal fibrosis in 7 of 8 patients. The remaining one patient who had normal ALT and stage 2 fibrosis deferred treatment. Treatment was started in 13 patients with < stage 2 fibrosis, mainly due to increased ALT values or a family history of hepatocellular carcinoma.

**Conclusion:** A liver biopsy was helpful in selecting treatment for patients with mild ALT elevation. A majority of patients with CHB undergoing liver biopsy received antiviral therapy afterwards. A large proportion of patients undergoing liver biopsy with normal ALT and high viral load had significant liver fibrosis

Fibrosis stage on histology	0	1	2	3	4	Total
# of patients	5	15	10	5	7	42
# of treated patients	2	11	9	5	7	34

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### Role of Antigen Processing and Presentation Genes in Development of Acute and Chronic Hepatitis Viral Infections

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**Purpose:** Progression of viral infection to either acute or chronic state depends on the efficacy of the host immune response. Whereas acute viral hepatitis invites a vigorous, multispecific T-cell response, chronic viral hepatitis is associated with a weaker, narrowly focused response. Specific T-cell hyporesponsiveness in the later could be due to inefficient delivery of antigens to MHC class I molecules. Antigen processing and transport to MHC

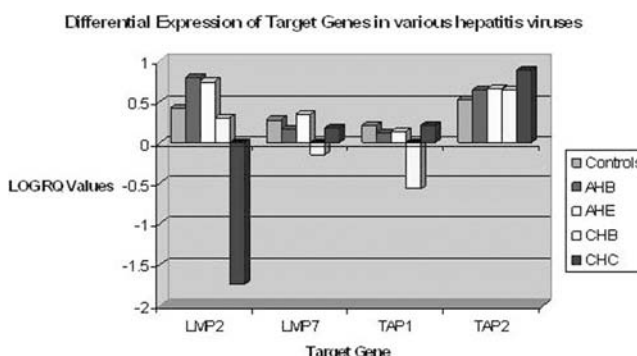
class I primarily involves, Low molecular weight protein (LMP); 2 and 7 and Transporter Associated with Antigen Processing (TAP) 1 and 2 genes. Immune system modifies this complex by addition of these subunits induced by IFN- $\gamma$ . We hypothesize that proteasome subunits shape the specific T-cell response and it may be dysfunctionally regulated in peripheral blood lymphocytes in chronic infections.

**Aim:** To investigate the expression of antigen processing and presentation genes in acute hepatitis B (AHB), acute hepatitis E (AHE), chronic hepatitis B (CHB) and chronic hepatitis C (CHC) patients.

**Methods:** Fifty subjects were studied: 10 of each category, AHB (age  $33.3 \pm 19.8$  yr., M = 7), AHE (age  $31.7 \pm 16.5$  yr., M = 7), CHB (age  $29.4 \pm 13.2$  yr., M = 8), CHC (age  $45.5 \pm 18.1$  yr., M = 8) and controls (age  $27.9 \pm 4.6$  yr., M = 7). Total RNA was isolated from PBMC's and cDNA was prepared and mRNA expression of TAP1, TAP2, LMP2 and LMP7 genes was quantified by Real-Time PCR.

**Results:** No significant difference in expression patterns between AHB and AHE was found. LMP2 was upregulated in AHB ( $P = 0.051$ ) and AHE (0.059) compared to controls. In CHC, LMP2 was significantly downregulated and TAP2 was upregulated in comparison to AHB and AHE. In CHB, TAP 1 and LMP 7 were significantly downregulated compared to controls and AH groups ( $P = 0.034, 0.006$ ).

**Conclusion:** i) Downregulation of LMP7 and TAP1 in CHBV and LMP2 in CHC suggests that the catalytic subunits of proteasome complex and antigen presentation genes play significant role in HBV and HCV persistence, ii) Similar profile in AHB and AHE suggests that while viral strains differ, acute hepatitis invites similar antigen processing pathways.[figure1]



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### Does the Stage of Fibrosis or Grade of Inflammation on Liver Biopsy Predict the Early Response to Combination Treatment with Pegylated Interferon and Ribavirin in Hepatitis C Patients?

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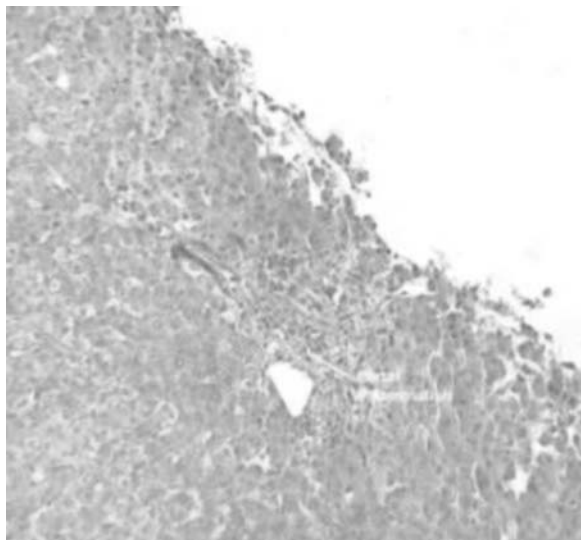
**Purpose:** Using the degree of fibrosis on liver biopsy as a component of the basis of therapy for hepatitis C patients is proven to be helpful in predicting response. Treatment is generally advised if the liver biopsy displays a Metavir score of more than or equal to 2 or an Ishak score of more than or equal to 3. There are no studies available which use the individual role of degree of inflammation or grade of fibrosis in predicting the response to treatment.

**Methods:** We conducted a retrospective chart review on 26 naive patients with hepatitis C genotype 1 [age 39–62 years] who were treated with the standard approved doses of combination Pegylated interferon and Ribavirin after having a liver biopsy. The early virologic response (EVR), defined as 2 log or more reduction in the viral count at 12 weeks of therapy, was calculated in each degree of inflammation group (1–4) and grade of fibrosis (1–4).

**Results:** The results showed that 53% of patients with grade 1&2 inflammation were initial responders to the therapy compared to 64% with grade 3&4. Initial responders of stage 1&2 fibrosis were 59% compared to 56% with

stage 3&4. Using Fisher's exact test the difference in the response rate was not statistically significant for both the grade of inflammation ( $P = 0.430$ ) and stage of fibrosis ( $P = 0.216$ ).

**Conclusion:** The EVR to treatment of patients with hepatitis C genotype 1 did not show a statistically significant difference between various degrees of inflammation or different stages of fibrosis on liver biopsy. Neither the stage of fibrosis nor grade of inflammation accurately predict treatment outcome in individuals. However these variables may be helpful in counseling patients and making treatment decisions.[figure1][figure2]



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### Primary Hepatic Lymphoma

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**Purpose:** Primary hepatic lymphoma (PHL) is a rare malignancy and constitutes about 0.016% of all cases of non-Hodgkin's lymphoma (NHL). PHL represents 0.4% of all extranodal non-Hodgkin's Lymphoma.

A 46 year old man with no significant past medical history, presented with two weeks history of jaundice, pruritus, epigastric and right upper quadrant discomfort, loss of appetite and 20 pound weight loss. On examination he

was jaundiced with mild right upper quadrant tenderness. The liver was enlarged to 5 cm below the right costal margin. No lymphadenopathy or splenomegaly was noted. Lab values were notable for total bilirubin of 14.1 mg/dl with direct fraction of 9.2, alkaline phosphatase of 646 U/L, GGT of 289 U/L, AST of 202 U/L, ALT of 87 U/L, albumin of 3.0 and LDH of 752 U/L. Alfa fetoprotein, CEA and CA 19-9 were not elevated.

Non-contrast enhanced CT of the abdomen showed a large hypodense mass in the left lobe of the liver. Contrast enhanced (early arterial phase) CT scan of the abdomen demonstrated a hypo vascular mass and minimal enhancement of the mass without distortion of the liver anatomy in the portal venous phase. Percutaneous liver biopsy revealed diffuse large B cell Lymphoma. Bone marrow biopsy was normal. Further workup did not reveal disease involvement elsewhere in the body. The patient was treated with combination chemotherapy. He responded well to chemotherapy and his liver functions normalized. After two years of follow up, the patient is asymptomatic with normal liver function tests and CT scan of the liver.

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### Safety of Bioelectrical Impedance Analysis in Evaluation of Patients with Liver Cirrhosis and Relation with Severity of Disease

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**Purpose:** Liver cirrhosis (LC) is characterized by pathological changes in homeostatic mechanisms which regulate the extracellular fluid volume. The changes of hydration status are estimate by Bioelectrical Impedance Analysis (BIA), a simple, inexpensive, non-invasive, patient-bed method. We evaluate the safety of BIA in LC.

**Methods:** We enrolled 48 patients ( $62 \pm 9$  yr, 27 male) admitted to our department with diagnosis of LC subdivided in three groups on the basis of Child-Pugh score (A group: 14 pts; B group: 17 pts; C group: 15 pts). There were no statistically significant differences in age and gender in each group. 16 healthy volunteers and 16 non-cirrhotic pts with a clear hyperhydration status (heart failure, kidney failure, nephrotic syndrome), matched for age and sex, were considered like controls. All the subjects underwent to blood tests, BIA-101 for detecting whole-body BIA measurements (Resistance: R; Reactance: Xc) and abdominal ultrasonography.

**Results:** Showed a significant reduction of parameters from A ( $R 537 \pm 33$ ,  $Xc 46 \pm 7$ ) to B ( $R 480 \pm 28$ ,  $Xc 38 \pm 6$ ) and C group ( $R 450 \pm 29$ ,  $Xc 35 \pm 5$ ). We observed a statistically significant reduction ( $P < .001$ ) between hyperhydrated ( $R 445 \pm 31$ ,  $Xc 36 \pm 8$ ) ( $R 544 \pm 33$ ,  $Xc 47 \pm 8$ ) vs. healthy controls measurements. No significant differences between hyperhydrated controls and B or C group was found. These results correlated inversely with Child-Pugh score ( $P < .001$ ), serum creatinine ( $P < .01$ ), directly with albumin ( $P < .01$ ), plasma sodium levels ( $P < .01$ ), hematocrit ( $P < .01$ ). When we classified the pts on the basis of ultrasonography presence of ascites not significant difference of bioelectrical parameters between moderate and tense ascites was found. Classifying the pts according to presence of ascites and to preserved or compromised liver function we observed a more significant reduction of these values ( $P < .001$ ) in ascitic pts with compromised liver function. Analyzing the subgroup of pts with ascites and normal BIA values we found that all had a preserved liver function.

**Conclusion:** BIA is a repeatable non operator-dependent method helpful for evaluation of hydration status in LC and correlates with clinical-functional class. Thus it is not capable of estimating the entity of ascites because it is a compartmentalized edema. However this method is useful for rapid evaluation of severity of disease and selection of pts with ascites for diuretic treatment (lower BIA values) or paracentesis (normal BIA values).

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### Toward Better Prognostic Modeling in Acute Liver Failure

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**Purpose:** Previous prognostic scores in ALF have reasonable specificity but inadequate sensitivity. To improve predictions, we explore a new model system that controls for the variable of coma severity.

**Methods:** Prospective data from more than 1,000 ALF patients enrolled in the United States ALF Study were used to explore whether basic lab values at time of progression to encephalopathy stage II or III, rather than at hospital or study admission, might be more useful in predicting outcomes. We also grouped patients according to ALF etiologies associated with favorable (acetaminophen, hepatitis A and ischemia) versus unfavorable (all other causes) outcomes. In separate logistic regression analyses we used standard laboratory measures from the first hospital day that stage II or III encephalopathy was reached. Patients with missing data for any variable included in the model were excluded. Pairs of logistic regression models used lab values and etiology groups to predict the following: death versus survival at 3 weeks, death or transplantation versus transplant-free (spontaneous) survival at 3 weeks, and transplantation versus no transplantation at 3 weeks.

**Results:** Well-fitting models were developed using standard laboratory parameters (Table). At arrival to coma grade II or III, death or transplantation was associated with higher Cr, INR, and total bilirubin, lower pH, and unfavorable etiology compared with spontaneous survival.

**Conclusion:** Using basic lab values at time of initial coma progression to stage II or III may yield more accurate prognostic models. Grouping by etiology is also important. Such a prognostic score should be clinically useful since predicting need for transplant is crucial at the time of listing, usually at or near grade II or III.

The US Acute Liver Failure Study Group is supported by U-01 58369; JP is the recipient of an ACG Research Award.[figure1]

First Coma Grade	Variables	Odds Ratio and p-values for predicting:					
		Dead (vs. Alive)	Wald's p-value	Transplant (vs. no transplant)	Wald's p-value	Death or Transplant (vs. alive without transplant)	Wald's p-value
3 or higher	Creatinine	1.24	<0.0001			1.16	0.0042
	INR	1.13	<0.0001			1.24	<0.0001
	Total Bilirubin					1.07	<0.0001
	pH	0.14	0.0070			0.07	0.0023
	Group (others vs. APAP, HepA, Shock)	1.46	0.0308			2.85	<0.0001
	c Statistic	0.68				0.78	
2 or higher	Creatinine	1.22	<0.0001			1.16	
	INR	1.15	<0.0001	1.09	0.0006	1.23	<0.0001
	Total Bilirubin			1.03	0.0002	1.06	<0.0001
	pH	0.17	0.0142			0.11	
	Group (others vs. APAP, HepA, Shock)	1.59	0.0057	4.12	<0.0001	3.21	<0.0001
	c Statistic	0.677		0.762		0.783	

had a liver biopsy prior to starting interferon therapy. We retrospectively reviewed the medical records of these patients to access their clinical as well as pertinent biochemical laboratory results. Liver biopsies were retrospectively reviewed by a single pathologist blinded to the clinical and laboratory findings.

**Results:** There were 67 patients in our study cohort. The mean age of the patients was 46.3  $\pm$  6.3 years. Of the 67 patients, 36(54%) were males and 31(46%) were females. An early virologic response defined as at least a 2 log(10) reduction in HCV RNA or HCV RNA negativity by week 12 was present in 73.7% of the patients while 57.8% of the patients had a sustained viral response. On univariate analysis, absence of EVR ( $P = 0.0002$ ), Non-white race ( $P = 0.008$ ), AST/ALT ratio  $\geq 1$  ( $P = 0.008$ ), INR  $\geq 1$  ( $P = 0.02$ ) and presence of steatosis  $\geq 5\%$  ( $P = 0.03$ ) on liver biopsy were negative predictors associated with SVR. In multivariate analysis, only absence of EVR, Nonwhite race, AST/ALT ratio  $\geq 1$  and presence of steatosis  $\geq 5\%$  were significant independent predictors of nonresponse to treatment.

**Conclusion:** In conclusion, the treatment rates and options for chronic HCV infection remain suboptimal. Absence of EVR, Non-white race, AST/ALT ratio  $\geq 1$  and presence of steatosis  $\geq 5\%$  on liver biopsy are independent negative predictors of sustained viral response rates of patients with Chronic HCV infection on treatment.

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#### Hepatic Infarct Following TIPS with a ePTE-Covered Stent and Review of the Literature

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**Purpose:** TIPS (transjugular intrahepatic portosystemic shunt) is an accepted therapeutic modality for gastrointestinal bleeding from portal hypertension that cannot be controlled by either endoscopic or pharmacologic therapy. TIPS should not be undertaken lightly, because the overall procedure-related mortality can be as high as 1% to 2% and complications including hepatic encephalopathy, portal vein thrombosis, sepsis, stent migration or stenosis, and intraperitoneal hemorrhage can occur. Expanded polytetrafluoroethylene (ePTE) covered stents have been developed to improve shunt patency and reduce TIPS malfunction. On review of the literature, there has been limited data analysis evaluating the potential for hepatic venous outflow obstruction related to covered stents with most of the information obtained from case reports. This abstract presents an interesting case of a segmental hepatic infarct after TIPS procedure using a GORE VIATORR covered stent.

**Methods:** A 67 y.o. male with hepatitis B cirrhosis and a history of decompensation with a gastric variceal bleed was scheduled for an outpatient TIPS

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#### Clinicopathological Predictors of Sustained Viral Response Rates in Patients with Chronic Hepatitis C Infection

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**Purpose:** Despite major progress made in treatment of patients with chronic Hepatitis C virus (HCV) infection, a substantial number of patients fail to respond or relapse after peginterferon and ribavirin therapy. Peginterferon and ribavirin has an overall sustained viral response (SVR) rate of 54–63%. The aim of our study was to identify clinical, laboratory and pathologic predictors associated with a lack of sustained response to treatment in patients with chronic HCV infection.

**Methods:** From December 2002 to November 2005, we included all patients who had completed interferon therapy for chronic HCV infection and



procedure. An ePTE-covered stent was placed successfully with a hepatic venous pressure gradient drop of 14 to 6 mm Hg. The patient complained of mild RUQ and right shoulder pain following the procedure. Physical examination revealed some liver tenderness without evidence of peritonitis.

**Results:** Laboratory evaluation revealed severe transaminitis with AST and ALT >2,000; however, synthetic function was preserved. The patient did clinically well throughout a brief hospital course with a decrease in transaminitis and no evidence of liver failure. A triple phase abdominal CT scan performed 6 days following TIPS procedure revealed a right hepatic lobe posterior segment infarct.

**Conclusion:** Segmental hepatic infarct is a potential complication following TIPS with covered stents.[figure1]

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### Predictive Values of HOMA and Metabolic Syndrome by Different Definitions in Identifying NASH and Liver Fibrosis in a Population with High Prevalence of Obesity and Diabetes

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**Purpose:** Insulin resistance and related metabolic syndrome (MS) have been closely linked to nonalcoholic fatty liver disease (NAFLD). The progression from NAFLD to nonalcoholic steatohepatitis (NASH) occurs in substantial but yet-to-be determined percentage of patients. This study analyzes which definition of the metabolic syndrome (MS) is more predictive of NASH and liver fibrosis in population with high prevalence of obesity and diabetes.

**Methods:** Our cohort consisted of 65 consecutive patients referred for liver biopsy with clinical suspicion of NAFLD. Histology was assessed blindly by a pathologist and the clinical data was also collected in blinded fashion. MS was assessed based on WHO, ATP III, and IDF definitions.

**Results:** Of 65 subjects, 37 (56.9%) had NASH, 17 (26.2%) had simple steatosis and 11(16.9%) had normal biopsy. In relation to NASH, the strongest correlation was observed with WHO definition of MS ( $r = 0.386$ ,  $P < 0.001$ ) > ATPIII ( $r = 0.371$ ,  $P = 0.002$ ) > HOMA ( $r = 0.332$ ,  $P < 0.001$ ) > IDF ( $r = 0.283$ ,  $P = 0.021$ ). However, in association with fibrosis, HOMA index was most strongly correlated with degree of fibrosis ( $r = 0.493$ ,  $P < 0.001$ ) as compared to the established definitions of MS. Of the three, WHO showed the strongest correlation with fibrosis ( $r = 0.411$ ,  $P < 0.001$ ) as compared to ATPIII ( $r = 0.36$ ,  $P < 0.001$ ) and IDF ( $r = 0.279$ ,  $P = 0.013$ ). After adjusting for age, AST, ALT, AST/ALT ratio and diabetes, HOMA index remained significantly associated with NASH as well as degree of fibrosis (OR: 7.3(2.2–24.4)  $P = 0.001$  and 13.1(2.5–69)  $P < 0.001$  respectively). All three definitions of the MS remained significant in relation to fibrosis [OR (95% CI) ATPIII: 9.1(1.8–45.0)  $P = 0.007$ ; WHO: 6.9(1.7–27.7)  $P = 0.007$  and IDF: 3.9(1.03–14.4)  $P = 0.044$ ]. While WHO and ATPIII remained significantly associated with NASH [OR: 8.4(2.0–34.5)  $P = 0.003$ ; and 6.3(1.8–22.0,  $P = 0.004$  respectively], IDF failed to remain significant [OR = 3.1(1.0–10.0)  $P = 0.057$ ] after adjusting for confounding factors.

**Conclusion:** HOMA and MS are significantly associated with NASH and liver fibrosis in patients with suspected NAFLD. While the WHO and ATPIII definitions were strongly predictive of NASH, IDF seemed inappropriate in identifying the likelihood of having NASH in patients with NAFLD.

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### Overview of Hepatitis A in Republic of Armenia

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**Purpose:** In etiological structure of viral hepatitis, the Hepatitis A (HA), during 1984–2003 averaged 87.3%. It is known, that disease can have sub-clinical course, especially at children. Basically, disease comes to an end recovery, however can be severe and even fulminant courses, with development of symptoms of an Acute Hepatic Encephalopathy (AHE) and a lethal outcomes.

The research problem is HA percent definition in patients with viral hepatitis, determination of age-specific characteristics, correlation of severity forms and HA evaluation in acute fulminant hepatitis.

**Methods:** A retrospective analysis of patients with viral hepatitis hospitalized into the Infectious Hospital during 2002–2006 was performed. The diagnosis of HA was formed based on epidemiologic evidence, clinical course of diseases, blood biochemical analysis data and anti-HAV IgM testing. Moreover, patients blood had been tested to HbsAg and anti-HCV.

**Results:** Of all 1919 patients with viral hepatitis, HA was confirmed in 944 (49%) patients. Male was 48.1% and female was 51.8%. All of patients had icteric form of HA. Of them in 12 (1.3%) was diagnosed mixed Hepatitis, at that HAV+HBV was in 7 patients and 4 patients had HA on the background of the chronic HCV infection. Age of patients was from several months till 76 years. Patients in age from 6–15 and 16–25 made up the most numerous group: 38.6% and 30.6% respectively. Children up to 6 years old were 6.8%, persons over 46 years old – 2.1% and practically did not suffer from HA children under 1 years – 0.3% only. Patients admitted to the Hospital during the whole year, but the most all in autumn-winter season. So during November – March admitted 532 (56.9%) patients with HA.

In 87.7% patients clinical course was moderate-severe, in 8.8% – severe and in 3.5% – mild. Fulminant course of hepatitis with AHE was in 4 (0.4%), at that 3 (0.3%) died due to hepatic coma. Age of patients with AHE was 10–47. All of them were hospitalized within first 10 days from the beginning of the disease.

**Conclusion:** Patients with HA are almost half of hospitalized patients with viral hepatitis. Persons in the age over 16 constitute 49% of HA diseased. The high percentage of patients with the moderate-severe form, probably, is conditioned by the fact that treatment in a hospital get patients with the pronounced symptoms of disease. HAV can also be the cause of fulminant hepatitis, with a lethal outcome.

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### Genetic Variation in the Peroxisome Proliferator Activated Receptor-gamma Gene Is Associated with NAFLD and Its Histological Phenotypes

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**Purpose:** Peroxisome proliferator activated receptor-gamma (PPAR- $\gamma$ ) is a nuclear receptor that regulates adipocyte differentiation, lipid metabolism and insulin sensitivity and is the molecular target for thiazolidinediones, agents that enhance sensitivity to insulin. Thus, it is a good candidate gene for NAFLD. The Ala12 variant of PPAR- $\gamma$  has been associated with increased insulin sensitivity, lower body mass and protection from type 2 diabetes. A second polymorphism C1431T has been associated with increased body weight.

**Aim:** To test the association of two PPAR- $\gamma$  single nucleotide polymorphisms (SNP) with NAFLD and its histological sub-phenotypes.

**Methods:** DNA was extracted from 158 archived, formalin-fixed liver biopsy specimens from patients with NAFLD and normal controls. Two SNPs of PPAR- $\gamma$  (Pro12Ala and C1431T) were genotyped by Taqman assay using the Biotrove OpenArray system. PPAR- $\gamma$  haplotypes were predicted using the program Dandelion, which employs the Expectation-Maximization (EM) algorithm to obtain maximum likelihood estimates of the haplotype frequencies and the probabilities of the observed haplo-genotypes for each individual.

**Results:** DNA was successfully isolated and genotyped for 26 controls, 87 FL, and 45 NASH patients. For both SNPs tested, the minor allele frequencies were decreased in NAFLD compared to controls (10.8 vs 25% for C1431T, and 9.5 vs 17.3% for Pro12Ala). In subjects with NAFLD, the minor alleles were enriched in subjects with FL compared to those with NASH (12.5 vs 7.5% for C1431T and 13.3 vs 0.03% for Pro12Ala). Only variation in C1431T was associated with steatosis ( $P$  0.03). Haplotype analysis revealed a haplotype consistent of both minor alleles (TG) that is present only in subjects with NAFLD but not in controls (2.7 vs 0%). This haplotype was also significantly associated with steatosis, fibrosis, ballooning and lobular inflammation under an additive genetic model.

**Conclusion:** Genetic variation in PPAR- $\gamma$  is associated with NAFLD and its histological phenotypes. A haplotype shows strong association with histological findings of NASH, and is more common in individuals with NAFLD than controls. This haplotype may influence the development of NASH and its characteristic inflammatory and fibrotic changes.

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#### Detection of Caspase Activity in the Plasma of Patients with Various Liver Diseases as a Novel Biomarker of Hepatic Fibrosis

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**Purpose:** Development of a reliable non-invasive test to predict liver fibrosis is greatly needed. The expanding knowledge about hepatocellular apoptosis as a prominent pathological feature in different liver diseases and its suspected role in triggering fibrosis supports apoptosis as a target for biomarker development. We have recently demonstrated that caspase 3-generated cytokeratin 18 (CK-18) fragments' level in blood is an independent predictor of advanced fibrosis in patients with nonalcoholic steatohepatitis. The aim of our study was to determine the value of this novel biomarker for assessing hepatic fibrosis in different liver diseases.

**Methods:** Prospectively, 191 consecutive patients with various liver diseases or abnormal liver tests referred to our liver biopsy clinic were enrolled. On the biopsy day, demographic and clinical data were collected along with blood samples. Histology of all liver biopsies was assessed blindly by an experienced hepatopathologist and used as the gold standard method for fibrosis staging scored: 0 for no fibrosis; 1 for early fibrosis; and 2 for advanced fibrosis. CK-18 fragments' level was measured in duplicates using a specific sandwich immunoELISA assay.

**Results:** Patients with advanced fibrosis ( $N = 45$ ) had significantly higher CK-18 fragments' level than those without advanced fibrosis (Median (Q25, Q75): 414.4 (207, 748), 214 (122, 400);  $P < 0.001$ ). The odds of having advanced fibrosis increased with increasing CK-18 levels. For every 50 U/L increase in CK-18 fragments' level, the likelihood of having advanced fibrosis increased 5% (OR (95% CI): 1.05 (1.001, 1.1)). Nonetheless, CK-18 level in isolation appeared to be a relative weak predictor of advanced fibrosis in these patients with an area under the ROC curve estimated to be 0.67 (95% CI: 0.58, 76). We are in the process of constructing a clinical model for prediction of advanced fibrosis based on CK-18 levels in conjunction with other clinical and laboratory tests.

**Conclusion:** Plasma CK-18 fragments' level is increased in patients with advanced fibrosis from various types of liver diseases. Measurement of this marker in conjunction with other simple clinical and laboratory data may be useful to predict advanced fibrosis.

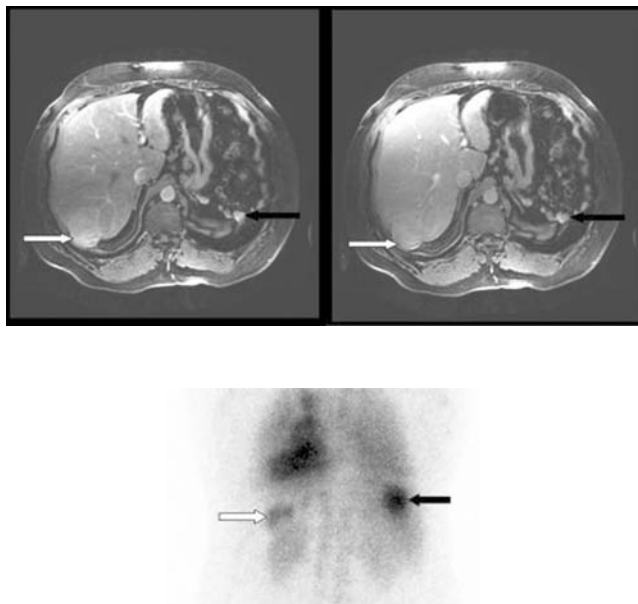
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#### Hepatic Splenosis Mimicking Hepatocellular Carcinoma

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**Purpose:** Splenosis is heterotopic implantation of splenic tissue after splenectomy or traumatic rupture of spleen. We report patient with alcoholic liver disease, who was found to have enhancing hepatic lesion during surveillance for HCC but was diagnosed as splenosis based on characteristic imaging, nuclear scintigraphic findings and associated multiple splenules. A 39-year-old man with alcoholic cirrhosis on routine surveillance for HCC was found to have small hypoechoic lesion on ultrasound, follow up MRI revealed a mass in right lobe of liver measuring  $4.5 \times 5.3$  cm with enhancement in early phase and an isodense lesion on late phase (white arrow in Fig. 1). These findings suggested a diagnosis of hepatocellular carcinoma. There were also multiple enhancing lesions in mesentery and splenic bud suggestive of splenules (black arrow in Fig. 1). A Tc-99m sulfur colloid scan showed uptake in the area of hepatic mass and splenules (marked with black and white arrow respectively in Fig. 2). Patient had splenectomy in past after abdominal trauma. Laboratory data revealed Alpha-fetoprotein 3.5, AST 58, and ALT 45. Six months later repeat imaging showed no increase in size of mass. In our case, the presence of concurrent mesenteric splenosis, normal alpha-fetoprotein, no growth on subsequent imaging and radio isotope uptake in liver and splenic bed on Tc-99m scan established the correct diagnosis of splenosis and averted the need for biopsy. Majority of the time splenosis is an incidental finding at surgery or autopsy, and at times discovered during computed tomography (CT) or magnetic resonance imaging (MRI). Splenosis being highly vascular mimics other vascular hepatic neoplasia and presents a dilemma in diagnosis of Hepatocellular carcinoma (HCC).[figure1][figure2]



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#### Transmission of Hepatitis B Virus (HBV) Infection Is Predominantly Perinatal in the Indian Subcontinent: A Large Prospective Study

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**Purpose:** India is in intermediate prevalence zone for HBV infection. Perinatal transmission is the predominant mode of transmission in high endemic

areas. HBV transmission in India is presumed to be predominantly horizontal, but there is scanty data. We conducted a study to test the hypothesis that chronic HBV infection in India is predominantly due to perinatal transmission.

**Aim:** To determine the source of HBV in chronic HBV infected patients.

**Methods:** Consecutive patients with chronic HBV infection whose relatives consented for evaluation were enrolled. Family tree was prepared and all available relatives were tested for HBsAg, anti-HBe, anti-HBs and total anti-HBc. Vertical transmission was defined when the mother was HBsAg positive or anti-HBe (suggestive of resolved HBV infection) and/or total anti-HBc positive (suggestive of past exposure). 254 healthy controls were also screened for comparison.

**Results:** 476 index patients (Age  $25.7 \pm 15.6$  yr; Males 363) had 1274 relatives available for screening. In 316 (66.4%) [Age  $20.2 \pm 14.3$  yr; Median (range) = 18(6 mo.-58 yr.); Males 251] index patients, mother could be screened. 226/316 (71.5%) mothers and 12/254 (4.7%) of controls were antibody positive (anti-HBe and/or total anti-HBc) ( $P < 0.001$ ), 133/316 (42.1%) mothers and 10/254 (3.9%) controls were HBsAg+ve ( $P < 0.001$ ) and 90 (28.5%) mothers were negative for HBV markers (Table). Of available 56 (17.7%) spouses (M:F::9:47), 25 (44.6%) were antibody positive (anti-HBe and/or total anti-HBc), 4 (7.1%) were HBsAg positive. Of 102 available siblings from 80 (25.3%) families, 27 (26.5%) were found to be antibody positive, 19 (18.6%) were HBsAg+ve.

**Conclusion:** Nearly 72% of chronic HBV patients in India acquire HBV infection through the mother. There is substantial evidence of present or past HBV infection in mothers of chronic HBV patients, suggesting possible perinatal transmission. Besides HBsAg, other antibody markers should be used to identify past HBV infection in the mother

Index patients whose mothers were positive for HBV markers (N = 226)

	Perinatal transmission	N	%
Mother HBsAg+ve & $\geq 2$ siblings HBsAg+ve	Definite	40	17.7
Mother HBsAg+ve & 1 sibling HBsAg+ve Or Mother antibody+ve & $\geq 2$ siblings HBsAg+ve	Highly likely	114	50.4
Mother antibody+ve & 1 sibling HBsAg+ve	Probable	72	31.9

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#### Are Ethnicity and Gender Associated with Outcomes in Patients with Primary Sclerosing Cholangitis (PSC)?

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**Purpose:** To evaluate the role of gender, ethnicity, age and clinical characteristics in the outcomes for PSC patients. Outcomes were defined as deaths, compared separately for those who underwent transplant and those who did not.

**Methods:** The medical records of patients diagnosed with PSC between March 1983 and December 2006 were reviewed. The diagnosis was documented using cholangiographical and/or histological and biochemical criteria. Data collected: age at diagnosis and transplant, gender, race, MELD at presentation, all laboratory data at presentation, and survival after transplant using chi-squared test, student t-test, and logistic regression where appropriate. Kaplan-Meier curves and cox proportional hazards models were used to compare survival.

**Results:** 56 patients were identified, 33(60%) males and 23(23%) females, 15(27%) blacks, 40(72%) whites. Mean age of diagnosis for blacks was 34.3 yrs compared to 45.4 yrs for whites ( $P = .001$ ). Total bilirubin (tBili) at pre-

sentation was higher for males compared to females (8.1 vs. 2.9 respectively;  $P = 0.01$ ). When stratified by race and gender, black males had significantly higher MELD scores than black females (19 vs. 12 respectively;  $P = 0.04$ ). No such differences were found between white males and females. 34 patients(61%) underwent liver transplant, 17 males and 17 females (28 whites and 6 blacks). The mean age at transplant for blacks was 42 yrs compared to 49 yrs for whites ( $P$ -value NS). 22 patients died during the follow-up period. Among those who underwent transplant, age at diagnosis was significantly associated with survival (HR 1.10; 95% CI 1.02–1.20;  $P = 0.027$ ). Median survival was similar among all groups. Among those that did not undergo transplant, age at diagnosis (HR 1.05; 95% CI 1.01–1.11;  $P = 0.04$ ), tBili at presentation (HR 1.05; 95% CI 1.01–1.11;  $P$ -value 0.008) and MELD score at presentation (HR 1.18; 95% CI 1.07–1.30;  $P = 0.001$ ) were associated with survival.

**Conclusion:** Black patients with PSC are diagnosed at a younger age. At presentation, black males have higher MELD scores and tBili than black females. Age at diagnosis is associated with survival after transplant. Age at diagnosis, MELD and total bilirubin at presentation are associated with survival for those that do not undergo transplant. Larger studies are needed to evaluate these factors.

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#### Patients with Hypertension and Diabetes Mellitus Undergoing Interferon Therapy for Treatment of HCV Are Not at Higher Risk To Develop Ophthalmologic Complications

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**Purpose:** To determine the frequency and risk factors related to interferon-associated ophthalmologic complications during treatment for hepatitis C.

**Methods:** Review of records from a cohort of patients undergoing HCV treatment between January 2005 and May 2007. Patients were treated with ribavirin in addition to either pegylated INF  $\alpha$ -2a,  $\alpha$ -2b or consensus INF. A mandatory, baseline ophthalmologic examination was performed on each patient prior to initiation of treatment. Data recorded included genotype, treatment duration, type of INF used, presence of prior eye disease/complaints, presence of DM / HTN, visual complaints during treatment and findings at baseline and follow-up eye exams. Any visual complaints during therapy prompted immediate evaluation by an eye specialist.

**Results:** A total of 183 patients treated for HCV were included in the study cohort. Seventy-one (38.7%) received interferon  $\alpha$ -2a, 100  $\alpha$ -2b (54.6%) and 12 (6.5%) consensus INF. Treatment duration was 1 to 48 weeks (mean = 27.6). Age range was 31 to 72 years (mean = 52.9) and 95% were men. Twenty-nine (15.8%) had DM, 85 (46.2%) HTN and twenty-one (12.5%) had both DM and HTN. One patient with DM + HTN had retinopathy (cotton wool spots) at baseline exam. During treatment 16 (8.7%) had visual complaints, but only 3/16 (18.75%) found to have retinal changes. In addition 4 (2.2%) asymptomatic patients had retinopathy on routine follow-up examinations. Overall 7 (3.82%), (6 during treatment) had documented retinal changes (6 CWS, 1 optic neuritis). Of 7 with retinal changes, 1 (14.2%) had DM, 3 (42.8%) HTN and 1 (14.2%) had both. Of these, 5 were on  $\alpha$ -2b and 2 on  $\alpha$ -2a. Three patients required treatment discontinuation 44, 20 and 2 weeks earlier than scheduled. These included asymptomatic worsening CWS(1), symptomatic CWS(1) and symptomatic optic neuritis (1).

**Conclusion:** In our study, both the incidence of symptomatic retinopathy and resultant treatment discontinuation rate appears very low 3/183 (1.63%) during treatment with PEG INF/ribavirin. The majority of patients who experienced visual symptoms during treatment had no evidence of retinopathy (81%). Diabetes and hypertension do not appear to be predictors for the development of clinically significant interferon-associated retinopathy.



## COLON

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**A Comparison of Polyethylene Glycol Laxative and Placebo for Relief of Constipation from Constipating Medications**

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**Purpose:** Medications often cause constipation and little data are available concerning treatment interventions. This study was designed to evaluate the safety and efficacy of polyethylene glycol (PEG) 3350 laxative (MiraLax) for relief of constipation from medicines associated with symptoms of constipation.

**Methods:** Study subjects were enrolled who met defined criteria for chronic constipation and were also taking medications that were associated with a reported side effect incidence of more than 3% constipation. Study subjects were randomized into a double-blind, parallel, multi-center study where they received 17 grams per day PEG laxative or placebo for 28 days. The primary efficacy variable, treatment success, was defined as relief of modified ROME criteria for constipation over the treatment period. Various secondary measures were also assessed. Daily bowel movement experience, patient perception of efficacy and safety information were recorded in a diary. Laboratory testing was performed at baseline and monthly for hematology and blood chemistry, including BUN, calcium, electrolytes, and TSH.

**Results:** 100 patients were enrolled in 4 study centers. Successful treatment according to the primary efficacy variable was seen in 78.3% of PEG and 39.1% of placebo subjects ( $P < 0.001$ ). Similar results were observed in a subgroup of 28 elderly subjects. Secondary measures of number of bowel movements, complete bowel movements, satisfactory bowel movements, straining at stool and stool consistency also showed statistically significant results in favor of PEG compared to placebo ( $P \leq 0.001$ ) after the first week of treatment. There were no differences in patient reported scores for gas, cramping, or bloating between PEG and placebo. No significant differences in laboratory findings or adverse events, including the gastrointestinal category, were observed. Diarrhea, flatulence, and nausea occurred more frequently with PEG treatment, although they were not individually statistically different from placebo. Similar results were observed when these symptoms were analyzed for differences due to gender, race, or age.

**Conclusion:** PEG laxative is safe and effective for use in treating constipation in patients taking constipating medications.

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**Expandable Metal Stents for Obstructing Lesions of the Colon as Bridge Therapy: An Alternative to Emergent Surgery**

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**Purpose:** Emergent colorectal surgery for colonic obstruction is associated with higher morbidity and mortality in comparison to elective non-emergent surgery. Endoscopically placed self expanding metal stents (SEMS) allow decompression of the colon and are used as palliative treatment obviating the need for surgery. The use of SEMS in the treatment of acute colonic obstruction in a resectable operative patient however has not been widely studied. We hypothesized that SEMS when used as bridge therapy prior to elective surgery for obstructing colon lesions (malignant or benign) would be a cost-effective strategy allowing for colon preparation, optimization of medical condition and a one-stage operation with resection and primary reanastomosis.

**Methods:** Review of medical records over a 4-year period identified 11 patients in Group A (mean age  $71 \pm 10.4$ , male 9, female 2) and 6 patients in Group B (mean age  $60 \pm 12.7$ , male 1, female 5). Two patients in Group A had benign strictures. Eight of 11 patients in Group A underwent

elective resection with primary re-anastomosis, 2 underwent resection with colostomy due to low-lying tumors and 1 patient expired (refused surgery). Two patients in group B had adenocarcinoma and 4 had benign strictures. Surgical interventions included sigmoidectomy with colostomy ( $N = 3$ ) and diverting loop colostomy ( $N = 3$ ). Procedural cost data were collected. Cost and complications of further surgical interventions in Group B were not included. Data were compared by the rank sum test and Chi squared test where appropriate.

**Results:** There were no technical difficulties in placing the stents. The mean duration between stent placement and elective surgery was  $37.5 \pm 57.0$  days. Mean survival in Group A was  $507.9 \pm 404.4$  days. One patient (9%) required SEMS removal due to stent migration post neoadjuvant chemoradiation. Two patients (33%) in Group B had post-operative complications. Mean survival in Group B was  $605 \pm 644.4$  days.

**Conclusion:** We conclude that SEMS followed by elective surgery for acute obstructive lesions of the colon in a resectable, operative patient is efficacious and more cost-effective compared to the traditional alternative of emergent surgery.

Cost-benefit analysis of SEMS and elective surgery versus emergent surgery				
Group	Cost (\$)	Morbidity (%)	Mortality (%)	Overall survival (mean, days)
A	2,500*	9.1	0	507.9
B	4,755	33.3	0	605.2

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**Views and Practice of Gastroenterologists Regarding High Fiber Diet and Fiber Supplementation in Patients with Colonic Diverticulosis**

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**Purpose:** There is no uniformity of practice about the role of high fiber diet (HFD) and fiber supplementation (FS) in patients with colonic diverticulosis (CD). We wanted to find out how many practising gastroenterologists recommend HFD & FS for patients with CD.

**Methods:** Members of AGA or ACG were contacted by phone or personal interview about their views & practices on this issue. The trainee members were not contacted. None of the physicians contacted declined to participate: participation was 100%. After the survey, information about the age of respondents was obtained from AMA & ABMS Directories. They were divided into 2 Groups: group I respondents were 49 years or younger; group II respondents were 50 years or older.

**Results:** There were 107 gastroenterologists in this survey. There were 11 (10.2%) women. The mean age was 53.0 yrs (range 32–95). Possible mechanism of CD in lay terms was discussed with patients by 16/107 (15%). 10/16 discussed it verbally; 2/16 (12.5%) gave written material; 4/16 (25%) gave both verbal & written discussion. 14/16 (87.5%) physicians themselves discussed it with patient & relatives; 2/16 (12.5%) cases nurses discussed it. 91/107 (85%) did not discuss the mechanism of CD; 47/91 thought patient would not understand it; 62 (68.1%) had no time for it. HFD was recommended by 67/107 (62.7%); 31/67 gave such instructions verbally; 13/67 (19.4%) gave written instructions; 23/67 (34.4%) gave both written & verbal. In 17/67 (25.3%) instructions by physician; 48/67 (71.6%) nurses & 2/67 (2.9%) times dietitians gave instructions. 40/107 (37.3%) did not give HFD instructions; 35/40 (87.5%) felt they were not effective & not needed; 8/40 (20.0%) had no time for it; 2/40 (5.0%) said it causes gas. Seedless diet was recommended by 34/67 (50.8%) of those who recommended HFD; 33/67 (49.2%) did not recommend seedless diet. FS was recommended by 55/107 (51.4%); 46/55 (83.7%) prescribed powder form; 9/55 (16.3%) prescribed capsules or tablets. 52/107 (48.6%) did not recommend FS; 28/52 (53.8%) felt it is not effective; 30/52 (57.6%) thought it causes gas. There were 43/107 (40.1%) in Group I; 64/107 (59.8%) in Group II. The mean age of Group I was 40.0 (range 32–49) yrs; the mean age of Group II was 60.0 (range 50–95) yrs. In Group I HFD was recommended

by 19/43(44%), in Group II HFD was recommended by 52/64(81.2%). FS was recommended by 16/43(37.2%) in Group I; it was recommended by 41/64(64.0%) in Group II. These differences are significant (Chi Sq,  $P < 0.05$ )

**Conclusion:** Majority of GI docs advise HFD & FS; significant minority do not. Younger GI docs less likely to advise HFD & FS. Powder form of FS most common.

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### The Effectiveness of Microscopic Colitis Treatments Based on Patient Demographics

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**Purpose:** Our aim was to create a preliminary study that analyzed the overlap or distinction between effective treatments for MC, LC and/or CC based on patient demographics and responses.

**Methods:** Pathology reports of 62 Patients diagnosed with MC, CC, or LC were compiled into a list from the Pathology department of United Medical Associates of Binghamton, New York. Patient demographic data were recorded into charts under the appropriate categories (LC or CC or MC). Responses to the nine treatments were recorded on a scaling system of 0–4, with 0 being No Response and 4 being Remission. The proper statistical tests were performed to find any significant difference in the demographics of patients with different types of colitis, average patient responses within the nine treatments, and average patient responses to each of the nine treatments between colitis types. The nine treatments were then organized into three categories (1-change in diet/fiber supplements; 2-over the counter; 3-prescribed). The proper statistical analysis was employed to find significant difference in average patient responses within the 3 treatment categories, and average patient responses to each of the above three categories between colitis types.

**Results:** 28 Patients (mean age =  $57.3 \pm 14.5$ ) have LC. 21 Patients (mean age =  $62.5 \pm 14.4$ ) have CC. 8 Patients (mean age =  $53.5 \pm 9.96$ ) have MC. 4 Patients (mean age =  $62.8 \pm 6.65$ ) have both LC and CC. 1 Patient has CC and MC. There was no significant difference in patient demographics between treatment groups, and between treatment responses for different colitis types for patients that underwent each of the nine treatments or the three treatment categories. There was a significant difference in average patient responses to Entocort treatment compared to responses to change in diet or responses to Imodium/Lomotil F(6,87) = 6.044,  $P < .05$ , and average patient responses to prescription drug treatment category compared to responses to over-the-counter medications or responses to fiber/change in diet. F(6,87) = 6.044,  $P < .05$ .

**Conclusion:** There was no correlation between types of colitis diagnosed, patient demographics and effectiveness of treatments. Entocort/Budesonide was a more effective treatment than diet change or use of anti-diarrhea medications, especially for CC patients. A larger prospective study is planned.

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### A Novel Artificial Magnetic Sphincter To Prevent Fecal Incontinence

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**Purpose:** Fecal incontinence due to low or absent tone of the anal sphincter represents, especially in the elderly, a problem that to date has not found yet a satisfactory solution in a not negligible number of patients (Br J Surg 2007;94:134). In this research we propose an original magnetic device to strengthen the hypotonic anal sphincter and prevent fecal incontinence.

**Methods:** The device consists in a couple of small magnetic plaques that are surgically inserted in the wall of the anal canal with the opposite polar-

ities face-to-face, so that, attracting themselves, close the anal lumen. The study was carried out in 3 swine anatomical preparations. Three couples of magnets of ovoidal shape made of materials of different magnetic force (neodimium>ferrite>plastroferrite) were tested. The magnets of each couple were inserted in two pouches on both sides of the anal canal between the external and internal anal sphincters. Each couple of magnets was tested in each preparation by doing, both before and after implantation, 3 trans-anal pull-throughs of a thin manometric catheter. The mean pressures obtained before and after magnet insertion were statistically compared with the Student  $t$  test.

**Results:** The endoanal pressure after the insertion of neodimium magnets was  $79.7 \pm 13.1$  mmHg (mean  $\pm$  SD), after ferrite magnets  $42.1 \pm 5.6$  mmHg and after plastroferrite magnets  $21.6 \pm 4.6$  mmHg, all of them significantly higher than the pressure recorded in basal conditions ( $1.72 \pm 0.71$  mmHg).

**Conclusion:** The present research demonstrated that the implantation of a couple of magnets in the wall of the anal canal is able to create a high pressure zone (HPZ), the value of which may be modulated by choosing magnets of various attraction force, so allowing a “tailored correction” of the anal sphincter hypotension. The main advantage of this system lies in the fact that the magnets create a “dynamic closure”, the mechanism of which has been previously demonstrated (J Biomechanics 2006;39:564): when the magnets are detached by the endoluminal pressure increase above the HPZ, they leave a passage that allows an easy transit of contents. Once verified “in vivo” in animals the effectiveness and tolerability of this system with magnets of proper strength covered by biocompatible material, this magnetic sphincter could represent a simple and effective solution of the fecal incontinence.

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### Intravenous Immunoglobulins for Clostridium Difficile Infection – A Systematic Review

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**Purpose:** Clostridium Difficile enterocolitis (CDE) responds promptly to oral metronidazole or vancomycin. Twenty to 35% of CDE patients though, develop refractory infection despite appropriate treatment; this may lead to colonic perforation, septicaemia and death (14%-25%).<sup>1</sup> Emergency colectomy (1.9%) in these circumstances is life saving.<sup>2</sup> However, some patients are unfit for colectomy due to co-morbidities; as well, the mortality rate from such intervention is extremely high (57%).<sup>2</sup> Leung et al., first in 1991, used intravenous immunoglobulin (IVIG) in six children with relapsing CDE with good results. Since then, IVIG was used for adult cases of CDE.

**Aim:** We conducted a systematic review in order to appraise the evidence for IVIG treatment of CDE.

**Methods:** Computerized search. We used the MeSH terms [Clostridium difficile] AND [immunoglobulins, intravenous]. Titles and abstracts were reviewed and full papers of those considered relevant were obtained. Reviews, editorials, letters and abstracts were not included.

**Results:** We found 7 case reports/series (28 subjects) and 1 case control retrospective analysis (18 subjects). A total of 46 patients received IVIG for refractory/recurrent CDE. Mean age of combined group was 70 years. The doses used range between 150 mg/kg to 500 mg/kg. For 12 patients (26%) multiple administrations (max. 6) were employed. We used three primary endpoint measures i.e. CDE related deaths, recurrence/relapse and colectomies. Therapeutic failure was 17.4% (8 deaths), 39.1% (18 relapses/recurrences) and 6.5% (3 colectomies), respectively.

**Conclusion:** Encouraging case reports for the use of IVIG in severe CDE, in conjunction with evidence of impaired immune response to Clostridium Difficile toxins in relapsing/recurrent CDE, have prompted more frequent use of IVIG. Despite similar recurrence and colectomy rates, the benefit of IVIG as salvage treatment for severe CDE is such to justify both its *ad hoc* use and prospective randomised control trials

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### Fermentation of Wheat Dextrin, Psyllium, and Inulin Are Altered but Not Improved by the Addition of *Lactobacillus reuteri*

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**Purpose:** *Lactobacillus reuteri* is a probiotic bacteria that has beneficial health effects when consumed orally such as decreased cholesterol, decreased diarrhea, and improved immunity. However, the interactions between *L. reuteri* and dietary fibers in the colon have not been extensively researched. This study characterized the effect *L. reuteri* has on the fermentation of wheat dextrin, psyllium, and inulin.

**Methods:** *In vitro* batch fermentation with human fecal inoculum was used to mimic colonic conditions. Wheat dextrin, psyllium, and inulin were incubated with added *L. reuteri* ( $\sim 10^{12}$  cfu/mL, LR+) or in the absence of *L. reuteri* (LR-). Samples were removed at 0, 4, 8, 12, and 24 hours for short-chain fatty acid (SCFA) analysis. Short-chain fatty acid concentrations were detected by GC-FID, and data was analyzed with SAS statistical software package (v.9.1).

**Results:** *L. reuteri* affected SCFA production by all fibers. Inulin LR+ had increased total SCFA, propionate, and butyrate concentrations at 4 and 24 hours, compared to inulin LR-. Inulin LR+ had decreased total SCFA, propionate, and butyrate at 8 and 12 hours compared to inulin LR-. Acetate production by inulin followed a similar trend, but was not significantly different at 12 and 24 hours. Psyllium LR+ had decreased total SCFA at 12 hours, decreased acetate at 12 hours, decreased propionate at 12 hours, and increased butyrate at 12 and 24 hours compared to psyllium LR-. Wheat dextrin LR+ had increased total SCFA at 8 hours, increased acetate at 4 and 8 hours, increased propionate at 4 hours, and increased butyrate at 4, 8, and 12 hours compared to LR-. LR+ favored butyrate production for psyllium (at the expense of propionate) and inulin (at the expense of acetate) at 24 hours. LR+ favored propionate production for wheat dextrin (at the expense of acetate) at 24 hours.

**Conclusion:** *L. reuteri* acts to improve different aspects of fermentation dependent on the type of fiber. Fibers should be combined with *L. reuteri* based on the desired fermentation pattern. Structural differences between the three fibers are likely the reason for differences in *L. reuteri*'s effects in fermentation. Wheat dextrin was steadily fermented, while psyllium and inulin were both rapidly fermented, suggesting more flatulence and bloating *in vivo*.

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### Prevalence of 5-ASA Use in Diverticulitis and Diverticulosis by Age and Gender

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**Purpose:** The purpose is to determine the prevalence of 5-ASA use in diverticular disease by age and gender.

**Methods:** This observational study used records of health service utilization from multiple US health plans within the Thomson Medstat MarketScan® research database. The subjects studied during the period July 2004 to June 2005 were  $\geq 18$  years of age with a diagnosis of diverticulitis (ICD-9: 562.11, 562.13) or diverticulosis (ICD-9: 562.10, 562.12). Inflammatory disease activity was determined by calculating the ratio diverticulitis prevalence to diverticulosis prevalence (D-ratio). 5-ASA use was defined as any use within 6 mos of diagnosis date. Subjects with a diagnosis of inflammatory bowel disease were excluded from the analysis.

**Results:** 2,109 (0.75%) patients were found to be on a 5-ASA from a total population of 281,665 patients with any diagnosis of diverticular disease. 5-ASA use was highest in the 18–29 age group. The ratio of diverticulitis to diverticulosis was highest among the youngest patients, particularly among males.

Prevalence Rates<sup>a</sup> of Disease and % 5-ASA Use by Age & Gender

Age Group (years)	Diverticulitis Male/Female	Diverticulosis Male/Female	D-ratio Male/Female	% 5-ASA Use Male/Female
18–29	0.53/0.21	0.56/0.32	0.95/0.66	1.65/2.15
30–39	2.14/0.92	2.25/1.45	0.85/0.63	0.88/0.88
40–49	3.97/2.67	7.44/5.76	0.53/0.46	0.67/0.88
50–59	6.13/5.84	27.78/24.45	0.22/0.24	0.52/0.76
60–69	7.72/9.66	40.15/39.54	0.19/0.24	0.58/0.79
70–79	8.97/12.55	46.78/47.96	0.19/0.26	0.79/1.03
80–99	9.51/12.43	40.65/37.94	0.23/0.33	0.82/0.94
Mean	58.6 yr/63.0 yr	62.6 yr/63.9 yr	0.25/0.28	0.65/0.87

<sup>a</sup>Rates per 1000 population

**Conclusion:** The higher ratio of diverticulitis to diverticulosis in the younger population reflects the more aggressive nature of the disease in this patient subtype. 5-ASA use occurs across all decades of patients with diverticular disease, albeit at a low level, but is highest in the younger patient population indicating increased usage in a subtype often associated with a more aggressive clinical course.

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### 5-ASA Treatment Practices among Physician Subspecialties in HIV-Associated Diarrhea

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**Purpose:** 5-ASA has recently demonstrated efficacy in HIV-associated colitis. Limited data exists on the pattern of 5-ASA use among physicians. The purpose of this analysis was to assess attitudes and patterns of 5-ASA use in chronic noninfectious diarrhea among different physician specialties.

**Methods:** 301 US physicians treating a large number of HIV(+) patients from 5 major geographical regions were surveyed from 2 specialties; primary care (N = 151; 89 internal medicine and 62 family/general practice; PCP) and infectious disease (N = 150; ID). Physicians were questioned on their 1st, 2nd, and 3rd line treatment practices for noninfectious HIV-associated

Table 1. Clinical Parameter

	PCP	ID
HIV patients per physician	170	221*
Chronic diarrhea prevalence	20%	13%*
Very concerned re:diarrhea	70%*	55%
Decreased incidence/5 years	36%	65%*
Currently use Asacol in these patients	38%*	13%
Likely to switch HIV therapies as a first line treatment for chronic noninfectious diarrhea	10%	25%*

\*P < 0.05

chronic diarrhea (HIV-ACD) along with the prevalence and relevance of the disease in their HIV patients.

**Results:** There were significant differences in HIV practice patterns (Table 1) and hierarchical use of 5-ASA between PCPs and ID physicians (Table 2). PCPs reported a significantly higher prevalence and concern for HIV-ACD than ID ( $P < 0.05$ ). This was associated with a significantly higher use of 5-ASA in the 1st and 2nd line of therapy. More than a third (38%) of primary care physicians use 5-ASA therapy for HIV-ACD, compared to only 13% of ID ( $P < 0.05$ ).

**Table 2.**

Treatment Options	PCPs (N = 151)			IDs (N = 150)		
	1st Line	2nd Line	3rd Line	1st Line	2nd Line	3rd Line
5-ASAs	15%	22%	25%	1%	1%	11%
OTC Medications*	91%	56%	21%	94%	61%	16%
No Treatment	1%	20%	1%	1%	28%	47%

\*Imodium (96% PCP, 98% ID); Lomotil (91% PCP, 95% ID); Bulk agents (89% PCP, 88% ID)

**Conclusion:** There is a significant disparity in the attitudes and therapeutic approach for HIV-ACD among PCP and IDs. Further research is needed to assess the reason for these differences.

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#### Colonoscopy with Withdrawal Times (WT) > 6 Minutes Detects More Polyps That Are Mostly Small and Hyperplastic (H) but Also a Few That Are Larger and Neoplastic (A)

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**Purpose:** Colonoscopy (C) is now an accepted standard as a screening test for colon cancer (CA). A recent published article demonstrated greater efficiency at polyp detection with colonoscopy withdrawal times >6 min. We

Description	Study Group	Control Group
age (yrs)	58 ± 12.5	58 ± 12.7
C with no polyps	137/300 (46%)	159/300 (53%)
C with any polyps	163/300 (54%)	141/300 (47%)
C with A polyps	104/300 (35%)	102/300 (34%)
C with H polyps	75/300 (25%)	49/300 (16%)
WT no polyps	6.58 ± 1.7 min	?????
WT with polyps	9.68 ± 3.2 min	?????
Polyps removed-total	322	263
Polyps removed-A	183 (57%)	175 (67%)
Polyps removed-H	112 (35%)	75 (29%)
cancer	5 (1.6%)	1 (0.4%)
other	22 (7%)	12 (5%)
Polyp size-<5 mm total	117 (36%)	52 (20%)
<5 mm-A	46 (39%)	24 (46%)
<5 mm H	61 (52%)	25 (48%)
<5 mm other (CA)	10 (0)	3 (0)
5-10 mm total	189 (59%)	202 (77%)
5-10 mm A	126 (67%)	144 (71%)
5-10 mm H	51 (27%)	49 (24%)
5-10 mm other (CA)	12 (1)	9 (0)
>10 mm total	16 (5%)	9 (3%)
>10 mm A	11	8
>10 mm H	0	0
>10 mm other (CA)	5 (4)	1 (1)

C = colonoscopy, A = adenomatous, H = hyperplastic, CA = cancer

hypothesized that the majority of polyps found would be small and hyperplastic.

**Methods:** 300 consecutive outpatient colonoscopies from Feb 2007 to May 2007 were evaluated and compared to 300 similarly aged colonoscopies from Feb 2006 to May 2006. All were performed by a single fellowship trained gastroenterologist. Study exclusions were incomplete colonoscopy, colonoscopy associated with complications, previous colonoscopy in the past 2 yrs, poor prep and previous colon resection. All 2007 colonoscopies had withdrawal times > 6 min as defined as the time from cecal identification to withdrawal across the anus. No withdrawal information was available for 2006 data but was assumed to be less than 6 minutes by experience. All polyps were measured and removed in a standard fashion.

**Results:** See table below.

**Conclusion:** Colonoscopy with withdrawal times > 6 minutes leads to higher polyp detection rates, especially for small (<5 mm) hyperplastic polyps. However, 4 additional cancers and 3 adenomatous polyps > 10 mm were seen in the study group over the control group. Since 4 of the 5 cancers were large and obvious, one must suspect an effect of sampling error. Repeating the study with a higher # of study patients would be beneficial.

### 374

#### Small (<5 mm) Right Sided Polyps (P) Are More Likely Adenomatous (A) Than Small Left Sided Polyps during Colonoscopy (C)

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**Purpose:** C with P removal is felt to be key in the reduction of colon cancer.

All P found during C should be removed. A recent article has been published showing a higher P detection rate with withdrawal times (WT) > 6 min. We thus set out to determine the distribution and pathology of the increased amount of P removed.

**Methods:** 300 consecutive outpatient C from Feb 2007 to May 2007 were evaluated and compared to 300 similarly aged C from Feb 2006 to May 2006. All were performed by a single fellowship trained gastroenterologist. Study exclusions were incomplete C, complicated C, previous C in the past 2 years, poor prep and previous colon resection. All 2007 C had WT > 6 min. All P were measured and removed in a standard fashion.

**Results:** 322 P were found in 163 study patients (SP) as compared to 263 P in 141 controls. Please see table for P distribution and path breakdown. In SP, 136 P were right (R) sided (cec/asc/trans) and 186 were left (L) sided (desc/sig/rec). In controls, 135 P were R sided and 128 were L sided. See table 2 for P information concerning <5 mm P only.

Location	All polyps removed	
	Study	Control
cec	34	27
<5 mm/5-10/>10	19/13/2	10/16/1
A/H/O/CA	25/5/4/1	19/6/2/1
asc	36	56
<5 mm/5-10/>10	13/22/1	11/40/5
A/H/O/CA	30/2/4/0	52/2/2/0
trans	66	52
<5 mm/5-10/>10	17/46/3	3/47/2
A/H/O/CA	57/6/3/1	47/3/2/0
desc	43	23
<5 mm/5-10/>10	10/31/2	4/19/0
A/H/O/CA	22/15/6/1	14/7/2/0
sig	75	57
<5 mm/5-10/>10	27/44/4	10/46/1
A/H/O/CA	36/35/4/0	33/22/2/0
rec	68	48
<5 mm/5-10/>10	31/33/4	14/34/0
A/H/O/CA	13/50/5/2	9/36/3/0

A = adenomatous, H = hyperplastic, O = other, CA=cancer

**Conclusion:** C WT >6 min leads to a higher P detection rate in almost all sections of the colon, but especially in the L colon. Small P (<5 mm) have a very high chance of being A in the R colon as compared to the L colon, especially the rec. Thus endoscopists should spend more time evaluating and removing small R sided P rather than small L sided P.

<5 mm polyps only				
Location	(Total #)	A	H	O
cec	S (19)	13	4	2
	C (10)	6	4	0
	CB (29)	19 (65%)	8 (28%)	2
asc	S (13)	9	2	2
	C (11)	11	0	0
	CB (24)	20 (83%)	2	2
trans	S (17)	15	2	0
	C (3)	3	0	0
	CB (20)	18 (90%)	2	0
desc	S (10)	3	6	1
	C (4)	2	1	1
	CB (14)	5 (36%)	7 (50%)	2
sig	S (27)	6	19	2
	C (10)	1	9	0
	CB (37)	7 (19%)	28 (76%)	2
rec	S (31)	0	28	3
	C (14)	1	11	2
	CB (45)	1	39 (87%)	5

S = study, C = control, CB = combined

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#### C-Reactive Protein and the Risk of Colorectal Adenoma in Apparently Healthy Populations

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**Table 1.** Comparison baseline characteristics between the control group and patients with colorectal adenoma

Characteristic	Control group (N = 3505)	Colorectal adenoma group (N = 1982)	P value
Mean age (years)	54.7 ± 6.6	62.3 ± 6.1	<0.05
Male-no (%)/Women-no	2074(59.1%)/1431	1404(70.8%)/578	<0.05
Current smokers-no (%)	590(16.8%)	310(16.1%)	0.471
Current user of post menopausal hormones	110(3.1%)	89(4.4%)	0.512
Women-no(%)			
Current user of aspirin -no(%)	511(14.5%)	220(11%)	0.184
Current user of multivitamins-no(%)	87(2.4%)	52(2.6%)	0.861
Body mass index-kg/m <sup>2</sup>	24.5 ± 2.8	25.0 ± 3.0	0.576
Fasting glucose (mg/dL)	100.0 ± 25.4	104.0 ± 30	0.431
C-reactive protein (mg/L)	1.4 ± 0.2	1.7 ± 0.25	0.126
Family history of colorectal cancer-no(%)	114(3.2%)	75(3.7%)	0.381

Values are expressed as mean ± SE. Current user of post menopausal women (%): percentage of the women taking the postmenopausal hormones in women. \*Probability value < 0.05 was considered significant.

**Purpose:** The purpose of this study is to evaluate the association between serum CRP levels and the risk of colorectal adenoma

**Methods:** 3505 normal control subjects and 1982 patients with colorectal adenoma were included in the study. The Mean level of CRP was compared between two groups, and correlation with other variations was analyzed by multiple regression analysis.

**Results:** There were significant differences in serum CRP level between two groups (Table 1). Multiple regression analysis revealed that the CRP level were not associated with the risk for colorectal adenoma (Table2).

**Conclusion:** CRP was not predictive of a higher risk for colorectal adenoma.

**Table 2.** Multiple regression analysis between the presence of colorectal adenoma and some variables including C-reactive protein

Variables	Regression	Standard	Chai-square	P
C-reactive protein	0.403	0.627	0.414	0.520
Age	0.086	0.020	16.899	0.021
Sex	-1.011	0.362	7.796	0.042
Body mass index	0.079	0.052	2.275	0.131
Fasting glucose	0.630	0.362	3.032	0.081
Smoking	2.417	0.871	2.934	0.087
Aspirin using	1.861	1.129	2.718	0.099
Postmenopausal hormone using	0.559	1.112	0.253	0.615
Multivitamine using	0.062	0.730	0.007	0.933

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#### Colonoscopy Scheduling for Elderly Patients: Morning or Afternoon Sessions and Does It Make a Difference?

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**Purpose:** Colonoscopy in the elderly can be a technically challenging procedure and it may result, in case of incomplete tests, in inconvenience and extra healthcare costs. Time of colonoscopy is an easily modifiable factor, if it proved to impact on the completion rate.

The aim of the study was to determine whether the time of a test (morning or afternoon session) impact on the success rate of cecal intubation.

**Methods:** We retrospectively reviewed all colonoscopies performed between March 2006 and 2007 in an endoscopy unit of a District General Hospital in UK. Patients aged ≥ 75 years old were considered as elderly. Time of procedure was classified as morning (if before 12:59 hr) or afternoon session (if after 13:00 hr) and preparation as good or poor, according to report.

**Results:** A total of 1885 colonoscopies was performed; (morning procedures 630, 347 [female] and 283 [male]; afternoon procedures 1255, 698 [female] and 557 [male]). Four hundred eighty three (483) were performed in elderly patients, ([female] 286, [male] 197) and 324 in afternoon sessions ([female] 196, [male] 128). In 284 patients (83 morning, 201 afternoon) examination failed cecal intubation (15%) and in 235 (12.4%) preparation was poor (78 in morning sessions). Higher incompleteness rate was found in elderly 93/483 (19.25%) vs. younger patients 191/1402 (13.6%),  $P < 0.05$  and among women 184/1045 (17.6%) vs. men 100/ 840 (11.9%),  $P < 0.001$ ; on the other hand, men ≥ 75 years old had worse preparation ([female] 28/286 or 9.9% vs. [male] 32/ 197 or 16.2%,  $P < 0.05$ ). Regarding the afternoon sessions, [female] ≥ 75 years old had higher cecal intubation failure rate than [female] < 75 years old (elderly [female] 46/196 or 23.4% vs. younger [female] 83/502 or 16.5%,  $P < 0.05$ ) and than elderly men, as well (elderly [female] 46/196 or 23.4% vs. elderly [male] 16/128 or 12.5%,  $P < 0.05$ ). No differences were observed in preparation either between sessions or between elderly and younger patients.

**Conclusion:** Afternoon colonoscopies have an impact on the completion rate, especially in elderly women. Scheduling these colonoscopies in morning sessions might avoid the need for further procedures.

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### The Association of Diabetes Mellitus and Colorectal Cancers

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**Purpose:** The aim of the study is to determine the association of diabetes mellitus with the subsequent development of colorectal cancer.

**Methods:** The endoscopy database at University of Florida /Jacksonville was reviewed retrospectively to identify all patients with masses discovered on colonoscopy from June 2003 to November 2005. Inclusion criteria were the presence of a colonic mass and a histologic diagnosis from the mass. Study subjects then had their medical records reviewed for the following information: age, gender, ethnicity, presenting symptoms for colonoscopy, presence of diabetes, body mass index, endoscopic location of masses and tumor stage. The data were analyzed using Chi Square & univariate analysis

**Results:** 230 patients who met inclusion criteria comprise the study population. Of the 230 colon masses, 134 were adenocarcinomas, 20 were normal mucosa & the rest were adenomas. Out of the 230 patients, 57 were diabetics & the rest were non diabetics. The mean age of the patients was 66.62. 123 patients were males and 107 were females. One hundred and nineteen patients were black, one hundred and six were white, three were Asians and two patients were Hispanics. Of the 230 patients with colon masses, 31 presented for colon cancer screening, 18 with heme positive stools, 76 with hematochezia, 24 with history of colon polyps, 42 with anemia, 14 with change of bowel habits, 3 with personal history of colon cancer and the rest had other reasons for colonoscopy (7 with abnormal CT scan, 8 with abdominal pain, one with family history of colon can & 6 with weight loss). Forty seven tumors were found in the rectum, 48 were found in the sigmoid colon, 20 were found in the descending colon, 31 in the transverse colon, 53 were found in the ascending colon, 30 tumors were found in the cecum and one mass was found in the anal canal. 39% of diabetics with colon cancer had cancer in the right side of the colon compared to 18.1% of non diabetics ( $P = 0.0462$ ) & 71.4% of diabetics with colon cancer had an early stage cancer (no lymph node /metastasis) compared to 50% of non-diabetics ( $P = 0.12$ ).

**Conclusion:** There was no association seen between DM and an increased risk of colorectal cancer. However, diabetic patients with colon cancer had proximal lesions more frequently than non-diabetic patients. DM patients were also noted to have a lower cancer compared to the general population. This may be due to the health care that diabetic patients receive in comparison to the general population.

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### ABSTRACT WITHDRAWN

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### Nurses Who Assist in Colonoscopy with Sedation On-Demand and a Novel Technique of Water Infusion without Air Insufflation Evaluate the Combination as Credible Options for Patient Care

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**Purpose:** We hypothesize that nurses (being patients advocate) can recognize impact of new options and methods on work load and are able to assess credibility of these for CRC screening.

**Methods:** Veterans underwent colonoscopy using sedation on-demand (SOD, at patients' request) and water infusion (without air insufflation) for CRC screening. 1. Procedure and recovery time in 30 randomly selected veterans who accepted SOD and their assessment of experience were tabulated. Satisfaction (0 = not satisfied, 10 = satisfied) was rated by veterans before discharge and at 24 hours. Their willingness to repeat was recorded. 2. Nine nurses provided anonymous evaluations of experience in assisting sedation on-demand and water infusion screening colonoscopy and completed 2 questionnaires using a 10 point scale (1 = no, 10 = yes).

Veterans Who Accepted Sedation On-Demand					
	Procedure Time	Recovery Time	Satisfaction Before Discharge	Satisfaction at 24 Hours	Willing to Repeat
Sedated (N = 15)	21.1 ± 2.5	27.7 ± 1.0	9.8 ± 0.2*	9.5 ± 0.2*	12 of 13*
Unsedated (N = 15)	18.9 ± 1.4	9.7 ± 1.0	9.9 ± 0.1	9.7 ± 0.2	14 of 15
P (unpaired t test)	NS	<0.05	NS	NS	NS

Data (mean ± SEM), time in minutes, \* 2 patients did not answer

**Results:** Recovery time was shorter for unsedated procedures (Table 1). Patients could be discharged sooner and this reduces nursing work load. Nurses' evaluations showed high credibility scores for both options (Table 2) **Conclusion:** Unsedated colonoscopy has shorter recovery time and reduced nurses' workload. Nurses witnessed the acceptance by veterans who reported high satisfaction scores and willingness to repeat. Both may have influenced the nurses' evaluations indicating sedation on-demand and technique of water infusion without air insufflation are credible options for patient care.

Nurses Evaluations		
Nurses Evaluation	Sedation On-Demand	Water Infusion Without Air
How logical?	9.3 ± 0.6	9.4 ± 0.3
Improve overall patient satisfaction?	8.2 ± 0.7	8.3 ± 0.6
Recommend to patients?	9.1 ± 0.6	9.4 ± 0.3
How satisfy are you when you assist?	9.0 ± 0.6	9.1 ± 0.3
Improve overall efficiency?	7.8 ± 0.8	8.3 ± 0.5
Overall credibility score (max = 50)	43.4 ± 2.7	44.7 ± 1.2

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### Poor Prep Rate for Inpatient Colonoscopies Is Unacceptably High – Needs Attention

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**Purpose:** Poor colon preparation (prep) is an important problem in both outpatients and inpatients. At our institution, as part of a quality improvement initiative, a series of interventions reduced poor prep rate from 18% to 1% in *outpatient colonoscopies* during 2002–2007. In this study, we have undertaken a *retrospective review of inpatient colonoscopies* to evaluate the incidence of poor prep and define the problem further so that quality improvement measures could be implemented to correct the problem.

**Methods:** **I. Incidence of the poor prep** was calculated in 850 consecutive inpatient colonoscopies compared to 5521 outpatient procedures (5/2005–4/2007).

**II. Descriptive analysis of 100 consecutive inpatient colonoscopies** with special reference to the quality of prep (5/2005–8/2005). [Statistical analysis was performed using SPSS v.11.0]

**Results:** **I. Incidence of Inpatient Poor Prep:** 27% (outpatients: 10%,  $P = 0.001$ ) [Odds Ratio 3.37, 95% CI 2.8–4.0]

**II. Descriptive analysis of 100 consecutive inpatient colonoscopies:** Mean age 61 years (range 25–96); male vs. female: 57 vs. 43; 22% had a prior colonoscopy; 97% received 4 liters of PEG based electrolyte solution. Indication of the procedure: diarrhea (6%), obscure bleeding (33%), overt bleeding (40%), & other causes (21%). Time of procedure: A.M. procedure in 68%.

**A. Quality of Prep:** Poor prep: 27% & Satisfactory prep: 73%. 1. Poor preps correlated with incomplete examinations ( $P = 0.001$ ), failure to establish a diagnosis ( $P = 0.002$ ). 2. No statistically significant association was observed between the quality of the bowel prep with relation to gender, indication for the procedure, a.m./p.m. colonoscopies, history of prior colonoscopies, and the presence of co-morbid conditions.

**B. Extent of Colonoscopy:** Cecal intubation was successful in 76% (complete examination). Patients with co-morbid conditions were at high risk of incomplete examination compared to those with none ( $P < 0.001$ ), irrespective of the quality of colon preparation.

**C. Financial Implications:** Repeat colonoscopy during the same hospitalization adds approximately \$3000 to the cost of care per patient.

**Conclusion:** The incidence of inpatient poor preps is unacceptably high (27%). Poor preps are associated with incomplete examinations and failure to establish the diagnosis. Repeat procedures increase the cost of patient care. Studies to define the problem and protocols to correct it are currently being established.

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### Excellent Cecal Cleansing with Split Dose of Phosphosoda and 30 mg of Bisacodyl – A Retrospective Study Using Cecal Photograph as a Reflector of the Quality of Colon Cleansing

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**Purpose:** Poor colon preparation was noted be 18% during an audit of the quality of colonoscopy preparation using polyethylene glycol based (PEG) solution in 2002. Since then, a series of changes have been made to our colon preparation protocol, which reduced the poor preparation rate to 8% & currently to 1%. *Cecum appears to be the last to get cleaned out and is often obscured by stools despite excellent cleansing of the rest of the colon.* Hence, 300 cecal photographs were graded to assess colon cleansing with different regimens by a single observer to avoid interobserver reporting bias. We also analysed the relationship between the quality of cecal image & colon polyp detection rate.

**Methods:** 100 consecutive colonoscopies in each group were compared.

**Group A:** 1 gallon of polyethylene glycol (PEG) the evening before procedure. **Group B:** 1.5 ounces phosphosoda (P) the evening before & 1.5 ounces on the day of procedure. **Group C:** Group B regimen + 10 mg of bisacodyl at noon and the evening before and on the day of procedure (P + BIS). **Assessment:** The cecal photograph was graded on a scale of 1–3: 1 = stool obscured the mucosa; 2 = 50–100% of mucosa visualized; specs of stool; 3 = Entire (100%) of the mucosa visualized (*excellent prep*); no stool.

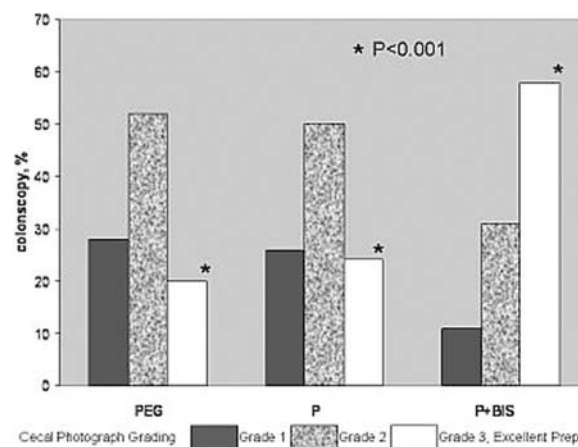
**Endpoints:** Mean colon cleansing (MCC) score & polyp detection for each preparation.

**Results:** **Excellent visualization of cecum (Grade 3) – Clean with 100% mucosal visualization:** 57% in the split dose of P + 30 mg BIS, 20% in the PEG, & 24% in the split dose of FP ( $P < 0.001$ ).

**MCC Score:**  $2.47 \pm 0.69$  in the split dose of P + 30 mg of BIS,  $1.98 \pm 0.71$  in the split dose of P, &  $1.92 \pm 0.69$  in the PEG respectively,  $P < .0001$ . The MCC score was higher in the P+BIS group in men ( $P < .0001$ ); females ( $P = 0.04$ ); age < 65 yrs ( $P < 0.0001$ ) &  $\geq 65$  yrs ( $P < 0.0001$ ).

**Polyp detection:** In the P+BIS group, there was a correlation between the quality of cecal image and polyp detection ( $P = 0.04$ ).

**Conclusion:** Using the cecal photograph as a reflector of the quality of colon cleansing, the split dose of phosphosoda & 30 mg bisacodyl proved to be superior to other regimens.[figure1]



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### Increased Risk of Colon Adenomatous Polyps in Patients Infected with Helicobacter Pylori

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**Purpose:** A recent meta-analysis suggested an increase in risk of colorectal cancers associated with *H. pylori* infection. However, because of selection biases, small sample sizes and inadequate consideration of potential confounding variables in the data analyses, publication bias cannot be ruled out. The aim of this study is to examine the relationship between *H. pylori* infection and colorectal cancer risk utilizing a larger sample size and a diverse group of patients at a single tertiary medical center.

**Methods:** We reviewed endoscopic gastric biopsy reports with positive *H. pylori* infection of all patients age greater than 40 years between January 2002 and January 2006 at our hospital. Pathology database was then reviewed for colorectal lesions found by colonoscopy within 6 years of checking *H. pylori* infection. Exclusion criteria consisted of age less than 40 years, gastrointestinal polyposis, history of malignancies and inflammatory bowel disease. Data were analyzed using t-test and chi-square test.

**Results:** There were a total of 410 patients in our data analysis. Of those, 173(42%) were *H. pylori* (+) and 194 (47%) were men. Mean age of the patient was 61.1 and 59.9 years in the *H. pylori* (+) and (-) group, respectively ( $P = \text{NS}$ ). In the *H. pylori* (-) group, 142(60%) patients had normal colonoscopic finding, 48(20%) had tubular adenoma and 0(0%) had adenocarcinoma. In contrast, in the *H. pylori* (+) group, 50(29%) had normal colonoscopic finding, 87(50%) had tubular adenoma and 1(0.6%) had adenocarcinoma. A statistically significant increase in the incidence of tubular adenoma was seen in the *H. pylori* (+) group ( $P < 0.0001$ ). In addition, among the *H. pylori* (+) group, significantly more men 63/95 (59%) than women 44/78 (41%) were seen with tubular adenoma ( $P = 0.008$ ).

**Conclusion:** *H. pylori* infection is associated with an increased risk of colorectal adenoma, specifically tubular adenoma. Men with *H. pylori* infection may need to have more frequent screening colonoscopy than current guidelines recommend.

	Helicobacter positive N = 173	Helicobacter negative N = 237	P value
Mean age (years)	61.1 $\pm$ 8.26	59.9 $\pm$ 7.54	NS
Females	78 (45%)	138 (58%)	0.009
Males	95 (54.9%)	99 (41.7%)	0.009
Adenocarcinoma	1 (0.6%)	0 (0%)	NS
Villous adenoma	1 (0.6%)	3 (1%)	NS
Tubulovillous adenoma	5 (2.9%)	6 (2.5%)	NS
Tubular adenoma	87 (50%)	48 (20%)	<0.0001
Hyperplastic	28 (16%)	38 (16%)	NS
Normal	50 (29%)	142 (60%)	<0.0001

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#### Quantitative Proteomic Profiling of Colorectal Cancer Stratified by Lymph Node and 8p LOH Status

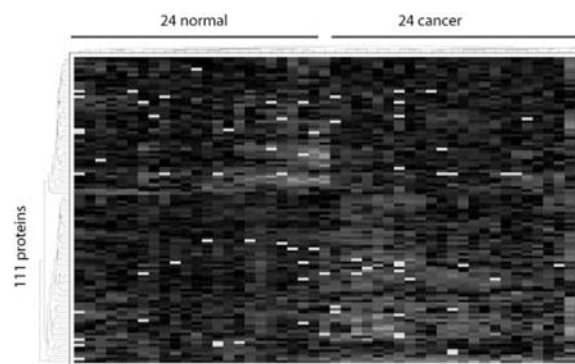
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**Purpose:** An objective of clinical proteomics, as applied to colorectal cancer (CRC), is to identify patients who are at greater risk of recurrence following initial resection and thus in need of more aggressive management. We applied sensitive proteomic technology to identify biomarkers that correlate with established prognostic indicators including lymph node status and LOH at chromosome 8p.

**Methods:** We compared 48 tissue samples: 12 node-positive CRC, 12 node-negative CRC, and patient-matched normal mucosa. Laser capture microdissection (LCM) was used to isolate pure cell populations from standard

frozen sections. About four micrograms of protein was analyzed by two-dimensional difference gel electrophoresis (2D-DIGE). About 200,000 data features were quantified, compared and analyzed using a Significance Analysis of Microarrays (SAM) procedure, which provides a list of candidate biomarkers ranked by priority. Mass spectrometry for molecular identification of candidate biomarkers is in progress.

**Results:** More than 2100 features per gel have been resolved. We project that about 1000 features will be matched as common across 90% or more of the gel images. Interim analysis of 604 well-matched features shows 111 with highly significant changes between cancer and normal (based on SAM analysis with estimated false discovery rate of <1%). A heat map in Fig. 1 shows an overview of the interim analysis. In addition, as compared between node positive and node negative samples, at least one feature has been identified to date. Characteristics of this and other candidate biomarkers will be discussed.[figure1]



**Conclusion:** The combination of LCM and 2D-DIGE provides a comprehensive approach for proteomic analysis of very small amounts of CRC tissue obtained from standard clinical specimens.

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#### Environmental and Dietary Risk Factors in Microscopic Colitis:

##### Preliminary Data from a Case-Control Study

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**Purpose:** To study environmental and dietary factors which may be associated with lymphocytic or collagenous colitis.

**Methods:** Cases were identified using a pathology department database queried for diagnostic terms and confirmed by an expert pathologist. Age & gender-matched controls were randomly invited from a database of routine visits to a university Family Care Center with satellite community clinics. A general questionnaire was completed on demographics, residences, employment, travel, animal exposures, infections, smoking, immunization, medications, and family history. A validated food-frequency questionnaire was used to record dietary habits over the past 1 year. Lymphocytic and collagenous colitis cases were analysed together. Statistical analyses included t-test for continuous variables, Wilcoxon rank-sum test for ordinal data, and Chi-squared or Fisher's exact test for categorical data. Significance was at  $P \leq 0.05$ . All protocols were first approved by the university ethics committee.

**Results:** Preliminary data on 38 subjects (23 cases, 15 controls) were available for demographics, residence, employment, animal exposure, smoking, immunization, family history and diet. Females comprised 78% of cases and 60% of controls ( $P = 0.28$ ). Mean age was 65.1 for cases and 57.5 for controls ( $P = 0.125$ ). Body mass was lower in cases (mean wt. 70.3 kg) than controls (mean wt. 87.7 kg) ( $P = 0.0009$ ). Cases had regular contact with dogs (96%) more often than controls (67%) ( $P = 0.027$ ) and had more regular contact



with fish as pets (43% cases, 0% controls,  $P = 0.028$ ). There were no differences in demographics, residence, employment or vaccinations. Cases more often reported (50%) a (+) family history of chronic diarrheal disease than controls (0%) ( $P = 0.002$ ). Cases ate less eggs ( $P = 0.037$ ) and processed meat ( $P = 0.049$ ) but more chicken ( $P = 0.042$ ) and seafood ( $P = 0.0007$ ) than controls.

**Conclusion:** This preliminary data of environmental risk factors show some associations with microscopic colitis and body mass, domestic pet exposures, family history of chronic diarrheal diseases, and meat consumption. The significance of these findings requires more investigation to determine which exposures preceded, rather than followed a diagnosis of microscopic colitis.

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### Relationship between Sporadic Hyperplastic Polyps and Colorectal Neoplasia in Hispanic Veterans

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**Purpose:** Hyperplastic polyps (HP) traditionally have been regarded as having no malignant potential. Some studies have suggested that HP in the distal colon may predict presence of adenomatous polyps in the proximal colon. Other studies have failed to show this relationship. The purpose of this study is to evaluate for the first time in our Hispanic veterans population if there is a relationship between the presence of sporadic HP and colorectal neoplasia (CRN) and to evaluate if proposed risk factors for CRN are also risk factors for sporadic HP.

**Methods:** The study consisted of a retrospective review of all the medical records of patients who underwent a colonoscopy for the first time at the VA Caribbean Health Care System during the calendar year 2005 and had a pathologic diagnosis of HP, tubular adenoma (TA), tubulovillous adenoma (TVA), villous adenoma (VA) and/or colon adenocarcinoma. Patient's age, BMI, smoking and alcohol use history, presence of DM, cholesterol and triglyceride levels, use of aspirin and the size and location of the lesions were recorded. Records with incomplete data and patients with a prior colonoscopy were excluded.

**Results:** 861 records were reviewed of which 405 records met the inclusion criteria (95% confidence interval). 99% of the patients were males, mean age 67.5 (36–87). 121 patients had HP, 331 had TA, 33 had TVA, 12 had VA, 13 had serrated adenomas and 61 patients had adenocarcinoma. The total number of colonic lesions was 1,065 (240 hyperplastic, 825 CRN). Univariate analysis using Pearson Chi-Square revealed that patients with HP appeared to have a lower likelihood of having TA ( $P < 0.001$ ), adenocarcinoma ( $P = 0.002$ ), and CRN in general ( $P < 0.001$ ). Multivariate analysis with logistic regression revealed that patients with HP had a significantly lower likelihood of having TA (adjusted OR = 0.21; 95% CI 0.12–0.37), and adenocarcinoma (adjusted OR = 0.33; 95% CI 0.15–0.73) compared to patients without HP. No correlation was found between DM, smoking, alcohol or aspirin use and the presence of HP.

**Conclusion:** This study demonstrates that sporadic hyperplastic polyps are not associated with CRN in the Hispanic veteran population. None of the risk factors proposed for CRN appear to be also risk factors for developing HP. The results of this study support current colon cancer guidelines in which surveillance for HP is not recommended.

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### Dyssynergia – Key Pathophysiologic Mechanism for Fecal Incontinence (FI) in Nursing Home Residents

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**Purpose:** We performed anorectal measurements in nursing home subjects to explain the high prevalence of coexistence of FI and constipation.

**Methods:** 16 subjects >80 yrs with FI underwent testing. A catheter with 3 solid state pressure transducers was placed in the anorectum with the subject in the left lateral position. Subjects were asked to squeeze as if to prevent fecal leakage and to strain as if to have a bowel movement. Rectal sensory thresholds were assessed by serial balloon distensions.

**Results:** All 16 subjects had normal rectoanal inhibitory reflex. 2 could not follow instructions, and 2 were not tested for strain-induced responses. All 12 who were able to strain showed either no relaxation or paradoxical contraction of the anal sphincter. 3 generated high intra-rectal pressure to produce defecation indexes of  $2.0 \pm 0.1$  that were normal ( $> 1.5$ ). The remaining nine (75%) showed a dyssynergic pattern with significant elevation of anal sphincter pressure and significantly reduced defecation indexes of  $0.9 \pm 0.1$ .

**Conclusion:** Nursing home residents with FI demonstrate weak internal and external anal sphincter pressures and severely impaired rectal sensation. Our novel finding (75% showing a dyssynergic pattern) could explain both the high prevalence of constipation and incontinence in these elderly nursing home subjects. [NIH1R02AG23555–01A1-JF Schnelle & VA Clinical Merit Research Funds-FW Leung].

Results	Mean $\pm$ SEM	Control
Sphincter length (cm)	$3.6 \pm 0.2$	2–4
Baseline intra-rectal pressure before squeeze (mm Hg)	$11.3 \pm 2.5$	
Peak intra-rectal pressure during squeeze (mm Hg)	$25.7 \pm 4.2^*$	
Baseline sphincter pressure before squeeze (mm Hg)	$22.4 \pm 2.3$	40–70
Peak sphincter pressure during squeeze (mm Hg)	$46.2 \pm 8.7^*$	100–180
Squeeze duration (seconds)	$8.5 \pm 1.8$	>30
Threshold for First sensation (ml)	$47.5 \pm 7.8$	10–30
Threshold for Urge to defecate (ml)	$99.4 \pm 12.5$	
Maximum tolerable volume (ml)	$165.0 \pm 14.5$	100–300
Baseline intra-rectal pressure before strain (mm Hg)	$17.1 \pm 2.9$	
Peak intra-rectal pressure during strain (mm Hg)	$51.0 \pm 7.8^*$	
Baseline sphincter pressure before strain (mm Hg)	$19.2 \pm 1.2$	
Peak sphincter pressure during strain (mm Hg)	$46.3 \pm 6.7^*$	

\*Vs. baseline before squeeze or strain,  $P < 0.05$ , paired t test.

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### Two Pathways of Carcinogenesis: MSI vs CIN in Iranian Patinets with Colorectal Cancer

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**Purpose:** Colorectal cancer (CRC) arising from a complex series of molecular changes that involve at least in two different pathways. These include microsatellite instability (MSI) pathway and chromosomal instability (CIN) pathway. The aim of this study was the determination of predominant pathway involved in carcinogenesis of patients with CRC less than 45 years old with and without family history (FH) of CRC.

**Methods:** In our study surgical pathology specimens of 108 patients with CRC less than 45 years old were immunostained for DNA mismatch repair proteins (MMRP) including hMLH1, hMSH2, hMSH6 and PMS2. Beta-catenin and P53 were also examined for CIN pathway

**Results:** Totally 108 patients with median age of 40(20 to 45) were evaluated. Fifty seven patients were male and 51 were female. The site of tumor in 84 patients was colon and in 14 were rectum. Among 96 patients with known family history, 33(34.4%) had positive FH. The overall rate of abnormal immunostaining were MLH1 8.3%, MSH2 18.5%, MSH6 8.3%, PMS2 11.1%, P53 74.1% and beta catenin 35.2%. Meanwhile abnormal staining for hMSH2 and hMSH6 were significantly more seen in patients with positive family history ( $P = 0.008$  and  $P = 0.032$  respectively). Patients with positive FH for CRC had significantly more abnormal MMRP (54.5% vs. 20.6%,  $P = 0.001$ ) and less positive p53 (54.5% vs. 81%,  $P = 0.006$ ) than patients with negative FH. Patients with early T, N stage tumor had at least one more abnormal MMRP than advance T, N stage ( $P = 0.050$  for T and  $P = 0.030$  for N stage). Among different factors abnormal hMSH2 had significant association with lower cancer related death ( $P = 0.040$ ). Patients with rectal cancer had more abnormal MMRP than patients with colon cancer but not significantly (35.7% vs. 29.8%,  $P = 0.655$ ) and positive p53 staining for rectal and colon cancer were 71.4% and 72.6% respectively. Both in colon and rectal cancer patients with negative family history had more prevalent positive p53 (80.4% vs. 56.7%,  $P = 0.022$  for colon and 81.8% vs. 33.3%,  $P = 0.099$  for rectal cancer).

**Conclusion:** Our study indicate that even in CRC less than 45 years old, the main pathway for carcinogenesis in patients with negative family history is CIN, but in positive family history MSI is as effective as CIN. However main pathway in both colon and rectal cancer is CIN.

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### Mismatch Repair Proteins and Clinicopathologic Factors in Colorectal Cancer

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**Purpose:** Microsatellite instability due to defective mismatch repair proteins (MMRP) is one of the major pathways for carcinogenesis in colorectal cancer (CRC). The impact of these proteins in prognosis is not well defined. The aim of this study were the evaluation of abnormal MMRP prevalence and its relationship with some clinical and pathologic factors.

**Methods:** In our study 350 CRC specimens were immunostained for DNA mismatch repair proteins (hMLH1, hMSH2, hMSH6, PMS2). Patients with at least one abnormal above factors considered in abnormal MMRP group. Clinical factors such as sex, tumor site, family history (FH) of CRC and vital status is considered. Pathologic factors including grade, T and N stage in tumor specimen were examined.

**Results:** 350 patients with median age of 51 were evaluated. The site of tumor was 270,68 in colon and rectum respectively. Among 329 patients with known FH, 132(40.1%) had positive FH. The overall rate of abnormal staining for hMLH1, hMSH2, hMSH6 and PMS2 were 4.4%, 7.2%, 3.5% and 4.9%. Overall 44 patients (12.7%) had at least one abnormal MMRP. Abnormal MMRP were not significantly associated with histopathologic factors (T, N stage, grade). Abnormal MMRP were seen further in colon than in rectum that was significant for hMLH1 ( $P = 0.044$ ). Patients with FH of CRC had more abnormal staining that was significant for hMSH2 ( $P = 0.041$ ). There was no difference in MMRP according to vital status.

**Conclusion:** Our results suggest that abnormal MMRP is associated with clinical factors such as family history of CRC but not with pathologic factors. Abnormal MMRP is more important pathway for carcinogenesis in colon than rectal cancer.

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### Constipation: Is It a Colonic Versus Generalized Gastrointestinal Tract Disorder. The Temple Experience

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**Purpose:** Constipation is a common clinical condition affecting millions of Americans. Its prevalence ranges between 2 and 28% depending upon the definition. When the physiology of chronic constipation is examined, four subtypes exist: slow transit constipation (STC), dyssynergic defecation (pelvic floor dysfunction; DD), a combination of both (STC + DD), and normal colon transit with normal pelvic floor function.

The purposes of this study were two-fold; first, to determine the percentage of constipated patients with STC, DD, STC+DD, or normal studies at a quaternary motility center; second, to evaluate what percentage of constipated patients have a diffuse gastrointestinal (GI) motility disorder as evidenced by a combination of upper and lower GI dysmotility.

**Methods:** This was a retrospective analysis of 488 patients who underwent anorectal manometry for the primary symptom of intractable constipation between 2001 and 2006 at Temple University Hospital's Motility Center. Of these patients, anorectal manometry, whole gut transit scintigraphy, anal electromyography, balloon expulsion testing, and defecography results were reviewed.

**Results:** Of the 488 patients with chronic constipation who underwent AM, 212 patients met the inclusion criteria for the study. Of these, 91/212 (43%) had STC, 25/212 (12%) had DD, 53/212 (25%) had a combination of STC+DD, and 43/212 (20%) had normal colon transit and pelvic floor function. Of the patients with STC, 31/91 (34%) had delayed gastric emptying, 9/91 (10%) had delayed small bowel transit, 7/91 (8%) had a delay in both, while 44/91 (48%) had normal upper GI motility. A similar distribution was seen in patients with DD – 8/25 (32%) had delayed gastric emptying, 2/25 (8%) had delayed small bowel transit, 2/25 (8%) had transit delays in the stomach and small bowel, whereas 13/25 (52%) had no abnormality. Examination of the STC+DD group showed 11/53 (21%) with gastric emptying delay, 7/53 (13%) with small bowel delay transit, 10/53 (19%) with a combination, and 25/53 (47%) had normal upper GI transit.

**Conclusion:** Patients presenting with a primary complaint of chronic constipation have a range of colonic motor disorders. The majority of patients had an identifiable abnormal pattern of colon transit, which included STC, DD, or a combination of STC and DD. In addition, many patients with chronic constipation have a generalized gastrointestinal tract disorder namely, delayed gastric emptying and/or delayed small bowel transit.

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### Utilization of Nitazoxanide for the Empiric Treatment of Diarrhea of Unknown Etiology

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**Purpose:** Diarrhea of unknown etiology is a common reason patients seek medical attention. While there are many reasons patients develop diarrhea, microbial insult has been targeted as a major contributor to this disease. Parasites, bacteria, and viruses are part of the spectrum of implicated organisms. Since testing for a specified organism is often inconclusive, costly, and untimely, clinicians often prescribe a trial of empiric antibiotics. Nitazoxanide (NTZ) is a first in class thiazolide antibiotic with activity against anaerobic bacteria, protozoans, helminthes, and gastrointestinal viruses. Furthermore, NTZ has a placebo-like safety profile, high gastrointestinal (GI) concentration, and limited to no activity against probiotic species. The purpose of this review is to evaluate the effectiveness of NTZ as empiric therapy for the treatment of diarrhea of unknown etiology.

**Methods:** A chart review was performed on patients treated with NTZ from April 2006 to April 2007 with complaints of generalized diarrhea not attributed to suspected small intestinal bacterial overgrowth (SIBO), or

*Clostridium difficile*-associated diarrhea (CDAD). Efficacy was measured as patient reported resolution of diarrhea or satisfactory improvement of symptoms by the end of therapy. Patients not returning to the clinic were contacted by telephone to determine resolution of symptoms. Twelve patients met the inclusion criteria for review.

**Results:** Of the 12 patients treated with NTZ, 9 were available for follow-up evaluation. Diarrhea was considered chronic or persistent in 8 of the 9 patients, one patient presented with acute diarrhea. The range of NTZ doses used was 500 mg BID-TID for 3–10 days, the mean dosing regimen was 1166 mg/day for 7.1 days. Overall 8/9 (89%) patients reported resolution of diarrhea or satisfactory improvement. Of note, the one patient failure had been prescribed NTZ 500 mg BID for 7 days, but the patient's insurance company would only allow the patient to receive 3 days of therapy (6 tablets). No clinically significant adverse reactions attributable to NTZ were identified during the study.

**Conclusion:** Nitazoxanide appears to be a safe and effective therapy for the empiric treatment of diarrhea of unknown etiology. Larger controlled clinical trials are warranted to support these findings.

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### Association of GSTM1, P1, T1 and CYP2E1 Single Nucleotide Polymorphisms with Colorectal Cancer in Iran

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**Purpose:** Colorectal cancer rate is very high and common cause of death. Mortality rate from colorectal cancer can be reduced by identification and removal of cancer precursors, adenomas, or by detection of cancer at an earlier stage. We performed this study to determine the association between genetic polymorphisms of cytochrome P4502E1 (CYP2E1) and glutathione S-transferases P1, M1 and T1 (GSTP1, M1, T1) and susceptibility to colorectal cancer (CRC).

**Methods:** Genotyping of CYP2E1 and GSTP1, M1, T1 was performed by using pyrosequencing analysis on DNA isolated from blood sample from colorectal cancer cases (N = 100) and normal controls (N = 100).

**Results:** Mean GSTT1 activity was significantly ( $P < 0.01$ ) higher in cases as compared to controls ( $P < 0.0001$ ; OR, 2.43; 95% CI, 1.47–4) on the other hand there is no significant association between GSTM1, P1, CYP2E1 and colorectal cancer.

**Conclusion:** GSTT1 measurement may be useful as a colorectal marker in colorectal cancer and biopsies obtained at colonoscopy can be used to measure tumor markers.

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### Development of Colon Cancer While in a Screening and Surveillance Program

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**Purpose:** Colon cancer is potentially preventable with screening and surveillance yet no program is 100% effective. We sought to characterize patients who developed colon cancer within 10 years of an index colonoscopy with or without other interval screening.

**Methods:** Retrospective review of patients diagnosed with colon cancer in 2001–2005. Electronic medical record was reviewed for a prior screening or surveillance colonoscopy performed within 10 years prior to cancer diagnosis. Exclusion criteria included high-risk patients (IBD and familial polyposis). Data extracted included location and stage of tumor, number and timing of previous colonoscopy and any limitations of the colonoscopy (poor prep or incomplete exam or incomplete prior polypectomy) and any other screening test (flexible sigmoidoscopy, fecal occult blood testing or colon x-ray).

**Results:** 294 pathology reports reviewed and 37 patients identified with a colonoscopy within 10 years of cancer diagnosis. 28 (76%) tumors were in the right colon with remainder (9, 24%) in the left. Cancers were stage 1 (32%), stage 2 (24%), stage 3 (38%) and stage 4 (5%). Patients were classified as to whether their follow-up was or was not in compliance with current ASGE guidelines. 13 patients were considered to have been potentially out of compliance for the following reasons; poor prep on index colonoscopy (N = 7, although 3 cancers were diagnosed on a repeat exam within one year of the index colonoscopy), prior incomplete polypectomy (N = 2) and adenoma > 1 cm without early follow-up (N = 4). The remainder (N = 24) were in compliance with current guidelines with 7 patients having small adenomas less than 3 years prior to cancer diagnosis, 2 having only hyperplastic polyps and 15 having normal exams all within 6 years of cancer diagnosis. In addition, 21 of 37 had additional screening tests in the 10 years prior to cancer development.

**Conclusion:** Screening and surveillance are important in the prevention of colon cancer yet some patients will develop cancer. Many, but not all may be prevented with better follow-up of patients with poor preparations or complicated lesions. Further study is needed to determine if the remainder of this problem is due missed adenomatous lesions or if these lesions have a more aggressive course with progression to cancer despite an appropriate screening exams and intervals.

The genotype frequencies of GSTM1, P1, T1 and CYP2E1 polymorphisms

Gene	Polymorphism	Wild		Heterozygous		Homozygous	
		Controls	Cases	Controls	Cases	Controls	Cases
CYP2E1	rs6413419(A/G)	95(95%)	80(88.9%)	5(5%)	10(11.1%)	0(0.0%)	0(0.0%)
CYP2E1	rs2854140(A/G)	88(96.7%)	83(96.5%)	3(3.3%)	3(3.5%)	0(0.0%)	0(0.0%)
GSTM1	rs17072289(A/T)	68(78.2%)	62 (87.3%)	18(20.7%)	8(11.3%)	1 (1.1%)	1 (1.4%)
GSTM1	rs1065411(C/G)	90(90%)	91(91.9%)	10(10%)	8(8.1%)	0(0.0%)	0(0.0%)
GSTM1	rs1056806(C/T)	87(87%)	91(91.9%)	13(13%)	8(8.1%)	0(0.0%)	0(0.0%)
GSTP1	rs1695(G/A)	53(53%)	54(54.5%)	42(42%)	39(39.4%)	5(5%)	6(6.1%)
GSTP1	rs4986948(G/C)	62(63.3%)	49(61.3%)	30(30.6%)	27(33.8%)	6(6.1%)	4(5%)
GSTP1	rs1138272(T/C)	83(87.4%)	53(72.6%)	12(12.6%)	19(26%)	0(0.0%)	1(1.4%)
GSTT1	rs2234953(A/G)	90(90.9%)	94(95.9%)	9(9%)	4(4.1%)	0(0.0%)	0(0.0%)
GSTT1	rs2266637(A/G)	37(52.9%)	34(37.4%)	26(37.1%)	26(28.6%)	7(10%)	31(34.1%)
GSTT1	rs4630(C/T)	100(100%)	79(98.8%)	0(0.0%)	1(1.3%)	0(0.0%)	0(0.0%)
GSTT1	rs2266633(A/G)	81(81%)	71(75.5%)	11(11%)	19(20.2%)	8(8.0%)	4(4.3%)

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**Effect of Exercise and Obesity on Difficulty of Performing Colonoscopy**

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**Purpose:** To prospectively look at different factors, which may predict difficult colonoscopy.

**Methods:** Consecutive patients undergoing outpatient colonoscopies were assessed for difficult colonoscopies. The main outcome variable, Time required to intubate the cecum, was used as a measure to assess the technical difficulty. Obesity was defined as body mass index of 30+. Exercise was stratified at 3+ times a week for 20+ minutes. Patient variables which were used as predictors of the main outcome were: age, sex, race, exercise, obesity, diverticulosis, pelvic surgery, alcohol use, and use of psychiatric medications.

**Results:** 128 consecutive patients were examined. 69 patients were obese. Obese patients took shorter time to reach the cecum (mean = 5.44 minutes) than non-obese patients (mean = 7.16 minutes). This was statistically significant ( $P = 0.0367$ ) at level 0.05. Only other variable that was statistically significant was Sex ( $P = 0.0134$ ), where reaching the secum took longer for women (mean = 7.21 minutes) than men (mean = 5.29 minutes). None of the other variables were statistically significant.

**Conclusion:** Patients who are obese may have easier exam than non-obese patients. Exercise has no effect on the level of difficulty in performing colonoscopy. Women have greater difficulty with colonoscopy than men. Our data clearly contradict anecdotal evidence.

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**In-Patient Colonoscopy Preparation – Is Splitting the Dose the Solution?**

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**Purpose:** Colon cleansing (prep) in the inpatient population continues to be a challenge for the Gastroenterologist. It is well known that the inpatient status is an independent predictor of inadequate colon prep. Due to multiple comorbidities, PEG-electrolyte lavage solution (PEG) remains the prep of choice in this population. In our center the standard 4-liter regimen has been shown to have 10% lower prep success rates compared to outpatients. Multiple studies in the outpatient population have shown split dose regimen of PEG to be superior. There is no published data assessing split dose regimen in hospitalized patients.

**Aim:** To evaluate the efficacy of prep for Colonoscopy using the conventional regimen of 4 L of PEG given the night before (Regimen 1) compared to PEG given 3 L the night before and 1 L the morning of the Colonoscopy (Regimen 2), and to compare the tolerability measured by the amount of PEG taken.

**Methods:** IRB approval was obtained for the study. After obtaining informed consent, patients were randomized using sealed envelopes. Baseline demographic data including co-morbidities were recorded. Endoscopist blinded to the regimen rated the colon prep. Rating was based on a validated scale from previous studies into 4 categories: Poor, Fair, Good and Excellent. Further, preps rated Excellent and Good were grouped as "Successful", Fair and Poor as "Unsuccessful". The amount of PEG completed was recorded by nursing staff.

**Results:** 85 patients have been enrolled to date, 3 patients were excluded: 1 underwent surgery, 1 emergent dialysis and 1 was discharged. 51% were male, 49% female. 46% were randomized to Regimen 1, and 54% to Regimen 2. Patients with Diabetes, hypertension, stroke, and Gastrostomy tube were equally distributed in both groups. 24% of patients in Regimen 1 had an "Excellent" overall prep compared to 56% of the patients in Regimen 2. 64% of the colon preps were "Successful" in Regimen 2, compared to a 36% of those in Regimen 1 ( $P = 0.038$ ). 16% of the patients in Regimen 1 had a "Poor" prep, compared to an 11% of those in Regimen 2 ( $P = 0.035$ ).

**Conclusion:** Split dose regimen is significantly better than conventional regimen in achieving successful colon prep in the inpatient population based on our preliminary analysis.

In-patient colonoscopy continues to be a challenge as the safety and efficacy is dependent on achieving an excellent prep. Splitting the dose of the PEG ensures tolerability and efficacy of colon prep in this difficult group of inpatients.

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**The Impact of BMI and Ethnicity on the Course of Colonic Diverticulitis**

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**Purpose:** To determine whether patients of different ethnic backgrounds have disparate courses of disease and to evaluate the role of obesity as a possible risk factor for virulent diverticulitis.

**Methods:** We conducted a retrospective chart review of 349 patients with confirmed diverticulitis in two university teaching hospitals in the Bronx, NY.

**Results:** Caucasians had a significantly greater risk (76.7%) than African Americans (52.5%) of developing a complication of diverticulitis on their initial admission for diverticulitis. African Americans were significantly more likely (26.1%) than either Hispanics (16.5%) or Caucasians (12.7%) to require surgery for diverticulitis after at least one medically managed admission for diverticulitis. A significantly greater percentage of obese patients (BMI > 30) than non-obese patients – 46.7% vs 35.2% – also were likely to have a recurrence of diverticulitis after an initial non-surgically treated episode. Non-Caucasians with a BMI < 30 also were more likely than Caucasians with a BMI < 30 to have a recurrent episode of diverticulitis after an initial medically-managed bout of diverticulitis (39.7% and 21.7%, respectively).

**Conclusion:** We demonstrated that the course of diverticulitis following one medically-managed admission for diverticulitis is more virulent in African Americans, as manifest by recurrence, the need for surgery, and development of complications. Caucasians, in contrast, have a more severe initial presentation of diverticulitis but a less severe course following an initial medically managed admission for diverticulitis than do non-Caucasians. Finally, we have established obesity as a risk factor for recurrence.

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**Fospropofol Disodium Is Effective and Safe for Sedation during Colonoscopy**

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**Purpose:** Fospropofol disodium (FP), a water-soluble prodrug of propofol, possesses a pharmacokinetic profile characterized by a smooth and predictable rise in propofol plasma concentrations that is unique from its active metabolite, propofol. This double-blind, multicenter, phase 3 study evaluated the safety & efficacy of FP 6.5 mg/kg & 2 mg/kg in patients undergoing colonoscopy.

**Methods:** 314 patients  $\geq 18$  years (ASA P1 to P3) were randomized to FP 6.5 mg/kg, FP 2 mg/kg, or midazolam (MD) 0.02 mg/kg in a 3:2:1 allocation following pretreatment with fentanyl 50 mcg. Patients were permitted to receive up to 3 supplemental doses of study drug before being considered a treatment failure & receiving an alternative sedative. Sedation was assessed using the Modified Observer's Assessment of Alertness/Sedation (MOAA/S). The primary endpoint was sedation success, defined by 3 consecutive MOAA/S scores of  $\leq 4$  after administration of sedative, and completion of the procedure without use of an alternative sedative medication & without

manual/mechanical ventilation. Other endpoints included measures of clinical benefit, recovery, memory retention, patient & physician satisfaction, and safety.

**Results:** Sedation success (87% vs 26%;  $P < .001$ ) was higher and the requirement for supplemental analgesic medication lower (55% vs 77%;  $P = .001$ ) in the FP 6.5 mg/kg group than the FP 2 mg/kg group. Patients in the 6.5 mg/kg group were less likely to remember being awake during the procedure (51% vs 100%;  $P < .0001$ ). The majority of patients in both groups reported willingness to use the sedative again (96% vs 91%). Patients in the FP 6.5 mg/kg group had higher memory retention (67%) than patients in the FP 2 mg/kg group (59%). Mean physician satisfaction scores were higher in the FP 6.5 mg/kg group (7.7) than in the FP 2 mg/kg group (4.5),  $P < .001$ . FP was well tolerated, with no serious treatment-related adverse events (TRAEs), deaths, or AE-related procedure discontinuations. The most common TRAEs in the FP 6.5 mg/kg and 2 mg/kg groups were paresthesias (68% vs 60%) and pruritus (16% vs 26%). Six patients experienced transient sedation-related AEs: FP 6.5 mg/kg (hypoxemia [resolved following repeated verbal stimulation,  $N = 1$ ], hypotension [ $N = 2$ ]); FP 2 mg/kg (hypotension [ $N = 2$ ]); midazolam (hypotension).

**Conclusion:** The FP 6.5 mg/kg dosing regimen is safe and effective for sedation during colonoscopy and is associated with a high level of sedation success, patient and physician satisfaction, and clear-headed recovery.

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#### Normal Anorectal Biomechanics Analyzed with Concurrent Intraluminal Manometry, Surface EMG and Fluoroscopy

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**Purpose:** Evaluations of patients with refractory constipation include defecograms to assess anorectal and pelvic floor (PF) function. Current interpretations are simplistic, involving assessment of anorectal angle and rapidity of emptying of barium paste. Our aims are to assess the coordination between anorectal pressures, change in rectal shape, and movement of rectal content, during a number of specific maneuvers designed to stimulate muscle groups relevant to anorectal function.

**Methods:** Surface electrodes were attached to the abdominal (AB) wall and to the perineum to measure from AB and PF muscle in 8 healthy female volunteers. Barium paste was inserted into the rectum and a 7F manometry catheter with 6 solid state transducers was inserted and taped in place to measure anorectal pressures. Fluoroscopy, pressure, and EMG were recorded simultaneously on a Kay Elemetrics workstation. The subjects conducted 5 maneuvers to isolate AB PF muscle contraction, including the Kegel and Valsalva maneuvers. Evacuation was measured with the fluoroscopy table upright. Pressures were analyzed as space-time isocontours, and in-house image analysis software was used to quantify the rectal boundary and rectal area during evacuation.

**Results:** In all subjects abdominal EMG (AB-EMG) contained periodic spikes with periods 0.63–0.75 s. Spike activity was not observed in PF-EMG. The Kegel maneuver was accompanied by well-defined spike activity in AB-EMG with minimal increase in baseline or rectal pressure, but baseline PF-EMG and sphincteric pressure increased significantly. By contrast, Valsalva displayed coordinated increases in EMG baselines, rectal and sphincter pressures. Fluoroscopy showed ascent of the PF with Kegel. With Valsalva the rectum stretched downwards as barium was forced into the anal canal. Evacuation was generally preceded by a period of anorectal pressure instability and rectal pressure increase. Evacuation was rapid, coincident with sphincter relaxation, and occurred as a two-part quasi-peristaltic contraction that separated the anorectal segment in two.

**Conclusion:** These preliminary data suggest that correlated space-time changes in anorectal pressure, EMG, and barium movement might distinguish normal from abnormal anorectal function.

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#### Antibacterial and Sporocidal Activity of Silver Against *Clostridium difficile* and Impact on Gut Colonization and Disease

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**Purpose:** To assess the activities of different forms of silver against the spores and vegetative cells of five strains of *C. difficile*, and to investigate the ability of silver-containing formulations to modify the course of *C. difficile*-associated disease in vivo.

**Methods:** The forms of silver included in this study were silver nitrate, silver (I) oxide, and NPI 32101, a nanocrystalline silver produced by physical vapor deposition using magnetron sputtering. Efficacy against vegetative cells of *C. difficile* was ascertained by a standard anaerobic MIC assay. Sporocidal activity was determined by exposing spores to test agents for intervals ranging from 15–120 minutes. Six days of subsequent negative culture was taken as an indication of sporocidal activity. The ability of silver to prevent *C. difficile* colonization and disease was determined by orally administering silver dispersions or control antibiotics to hamsters previously colonized with *C. difficile* after pre-exposure to clindamycin.

**Results:** The silver MICs against vegetative cells of five different strains of *C. difficile* ranged from 8 to 23  $\mu\text{g/ml}$ , which was significantly lower ( $P = 0.024$  by Mann-Whitney) than MICs obtained against other anaerobic species tested. Silver had sporocidal activity that required at least 15 minutes exposure to 50–500  $\mu\text{g}$  silver/ml. Sporocidal activity was more consistent after 1 hour of exposure. This was similar to the concentration- and exposure time-requirements for the positive control sporocidal agent, glutaraldehyde. In vivo studies demonstrated that a single oral dose of silver reduced colonization by *C. difficile* to an extent similar to a single oral dose of metronidazole, but not as well as a single oral dose of vancomycin ( $P < 0.05$  by Kruskal-Wallis, Tukey test). Importantly, pre-exposure of hamsters to nanocrystalline silver did not render hamsters susceptible to CDAD.

**Conclusion:** These data show that silver is bactericidal and sporocidal against *C. difficile*, and suggest potential utility as a first-line treatment for CDAD. This work was funded by Nucryst Pharmaceuticals, Inc., Wakefield, MA.

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#### Colon Cancer: Protein Biomarkers in Tissue and Body Fluids

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**Purpose:** The aim of the study was to validate the concept that potential biomarkers of colon cancer can be identified from body fluids. We concurrently tested multiple body fluid samples (urine, saliva, stool) and tumor tissue samples to identify concordant proteins. In our Institutional Review Board approved prospective pilot study, we explored the proteomic diagnosis of colon cancer by identification of concordant proteins in tumor and body fluids from the same patient.

**Methods:** After informed consent, body fluids and tumor tissue samples were obtained from 20 patients who underwent colonoscopy for tumor biopsy at The Brooklyn Hospital. Tissue and body fluids from patients with negative biopsies (10 subjects) were controls. The samples were frozen and transported to New York University School of Medicine, Department of Pharmacology for analysis. Proteins were extracted from tissue and stool with high pressure, 35K PSI, (Barocycler, Pressure Biosciences, Woburn, MA). Protein separation from tumor, urine, saliva and stool was performed with either Two-dimensional gel electrophoresis or HPLC (high performance liquid chromatography). Control and tumor samples were reduced (DTT), alkylated (iodoacetamide) and trypsin digested. The protein digests were applied to MALDI (matrix-assisted laser desorption/ionization) target plates for MALDI MS (MALDI mass spectrometry) and MALDI MS MS (MALDI tandem) mass spectrometry (Axima TOF, Shimadzu Biotech, Columbia,

MD). Protein were identified using NCBI nr data base interrogation with Mascot© software (Matrix Science, London, UK).

**Results:** The control sample MALDI MS spectra were all similar to each other as were the tumor sample spectra, however, there were clear differences between the MALDI MS control and sample spectra. Concordant proteins were identified from MALDI MS spectra in body fluids and tumor.

**Conclusion:** The apparent *tumor signature proteins* present in the body fluids could allow us to develop *non-invasive* clinical diagnostic tests of *colon carcinoma*. To prove the validity of these findings a larger molecular epidemiology study will be undertaken.

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### Do ACG Guidelines Still Predict C. difficile Diarrhea in Hospitalized Patients?

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**Purpose:** American College of Gastroenterology (ACG) guidelines published in 1997 provide criteria for patient selection for *Clostridium difficile* (C. difficile) testing. Since that time, C. difficile has become more prevalent in hospitals, more virulent, and new risk factors have been identified. Furthermore, these guidelines allow for repeat testing after an initial negative result despite a paucity of data supporting this practice. The purpose of this study is to determine whether the published guidelines effectively predict C. difficile infection among patients with multiple samples sent and to determine the yield of subsequent tests following an initial negative result.

**Methods:** Retrospective chart review of inpatients who had multiple stool samples sent to be evaluated for the presence of C. difficile toxin by enzyme immunoassay (EIA) between January and June 2005. Data were collected from daily progress notes, nursing flow sheets, medication records, and computerized physician orders.

**Results:** 144 patients had multiple assays performed during the study period. 93/144 (64.6%) met ACG guidelines at the time the first sample was sent for EIA testing; 88/144 (61.1%) met guidelines at the time the second sample was sent; 39/69 (56.5%) met ACG guidelines at the time the third sample was sent. When ACG guidelines were met on initial testing, 39/93 (33.3%) had positive test results for C. difficile toxin. This differed significantly from 9/51 (17.6%) patients with positive EIA results who did not meet ACG criteria for testing ( $P = 0.05$ ). Conversely, meeting ACG criteria on subsequent tests did not improve the likelihood of a positive result ( $P = 0.9$ ). Only 5/104 (4.8%) patients had an initial negative EIA test which became positive on subsequent testing.

**Conclusion:** Among patients who had multiple stool samples sent for analysis, meeting ACG guidelines improved the pretest probability of a positive test result for the first specimen sent, but not on subsequent specimens. Using ACG guidelines alone, however, failed to identify some patients who were, in fact, positive for C. difficile. In addition, the role of repeated testing for C. difficile after an initial negative EIA is of unclear benefit.

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### Chronic Constipation and Fecal Impaction: Novel but Effective and Economical Approach for Evaluation, Treatment and Prevention

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**Purpose:** To check "Carousel Theory" (putting more baggage on faulty airport carousel will not help it move and may even slow it down further causing baggage jam) for Chronic Constipation in Patients with Neurogenic Colon. Chronic constipation is traditionally treated with an advise to increase dietary fibers. However severely constipated institutionalized patients do not seem to respond well to this, even when the promotility drugs are added. I am suggesting a novel and effective strategy for a common problem that is

estimated to have \$ 7 billion dollar impact just on our nation and much more worldwide.

**Methods:** Total 70 Patients with history of chronic constipation were chosen for the study. Colonoscopy was scheduled to rule out any anatomical lesion and as a part of bowel preparation, they all were put on low fiber diet for two days before the test and were given PEG-3350 for two days. Many patients were found to have a surprising finding- their colon would hold about 800 to 1000 ml of the liquid preparation without any effective peristalsis. One group of these patients with Neurogenic Colon were put on low fiber diet and regular PEG-3350 and mild laxative. The other was given traditional high fiber diet. During follow up the groups were compared for- regularity and form of bowel movement, follow up abdominal x-rays, need for enema, need for manual disimpaction, as well as need for transfer to community hospital for constipation related work up and management.

**Results:** Contrary to popular belief, the group that was given low fiber was observed to have lower incidence for all the parameters checked.

**Conclusion:** This makes physiologic sense, that the colon that can hold 800 ml or more of liquid without generating any peristalsis, obviously can not generate enough peristalsis to propel solid and often hard stool formed by high fiber diet. Loading a neurogenic colon with fiber had adverse effect of bowel function therefore it should be limited.

The result of this observation from the institutionalized patients were duplicated in small number of community patients with similar results. but need to be duplicated in larger number of patients. If so, then patient education and relatively simple dietary modification can help many patients, save many dollars spent after new research and treatment for this worldwide problem.

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### Colonoscopy and Colography Are the Appropriate Terms To Use When Referring to the Endoscopic and Radiological Examination of the Lower Gastrointestinal Tract

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**Purpose:** The endoscopic examination of the colon is commonly referred to as *colonoscopy* and is currently the dominant modality for colon cancer screening, a major public health concern. It also forms the bulk of the current gastrointestinal endoscopic practice. The endoscopic examination of the colon is also referred to as *coloscopy*, especially in Europe.

Despite the evolution of endoscopy, a large proportion of the US population remains unscreened and attempts are being made to enhance compliance with colon cancer screening. Part of this effort is the development of the non-invasive, radiological study of the colon, which is interchangeably referred to as both *colonography* and *colography*. This shows that the rapid advent of new technology and procedures in the field of gastroenterology has resulted in the indiscriminate use of medical terminology.

Medical terminology is based on word construction and uses the concept of the *word root* in the context of the source language. By applying the rules of grammar and linguistics, we demonstrate that the desirable word root is *col-* (from the Greek *col-on*, meaning *the gut*) and not *colon-* (from the Greek *colon-os*, meaning *a hill*). The correct compound terms *col-oscopy*, *col-ography*, *col-itis*, *col-ectomy* and *col-ostomy* should therefore prevail over the corresponding terms *colon-oscopy*, *colon-ography*, *colon-itis*, *colon-ectomy* and *colon-ostomy* which would otherwise refer nonsensically to the examination of the hill, inflammation of the hill, surgical excision of the hill, etc.

With regard to the two aforementioned ways of examining the lower gastrointestinal tract, the only correct terms are therefore *coloscopy* and *colography*. Old habits die hard, and *colonoscopy* has already become the established term to describe the endoscopic examination of the gut. However, it would certainly be appropriate for the term *colography* to prevail over *colonography* when referring to the more recently developed radiological evaluation of the gut, e.g. in the form of CT colography, PET colography and virtual coloscopy.

### Screening Colonoscopy in Average Risk Afro-Caribbean Population below Fifty Five Years of Age

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**Purpose:** Recent studies suggest that colorectal neoplasia prevalence may differ in different population and it may be higher and may present earlier in African Americans. Committee of Minority Affairs and Cultural Diversity, American College of Gastroenterology issued new recommendations to begin colorectal cancer screening in African Americans at age 45 rather than 50 years. The prevalence of colorectal neoplasia in Afro-Caribbean population in the United States however is not known.

**Methods:** We retrospectively analyzed consecutive screening colonoscopy performed in asymptomatic average risk patients of Afro-Caribbean descent below 55 years of age over 6 month's period. The exclusion criteria included patients above 55 years of age, history of inflammatory bowel disease, previous history of adenoma or colorectal cancer and family history of colon cancer. Patients with hyperplastic polyps or inflammatory polyps on pathology were also excluded. The patients were analyzed for the size of the polyps (<5 mm, 5–9 mm, ≥10 mm), location of the polyps (proximal to the splenic flexure or distal to the splenic flexure) and histopathology. 95% confidence intervals were calculated using the exact binomial method.

**Results:** A total of 218 patients had screening colonoscopy between 50 years and 55 years of age (mean age of 52.2 years) during the study period. 65% of the patients were females and 35% were males. 46 patients (21%) [95% CI (15.9%, 26.8%)] were found to have adenomatous polyps, of these 7 patients (15%) had tubulovillous polyps. 31% of the males had polyps and 19% of the females had polyps. A total of 58 polyps were found, of these 33 (57%) [95% CI (43.6%, 69.67%)] were proximal to the splenic flexure and 25 (43%) were distal to the splenic flexure. 24 polyps (41%) were < 5 mm, 34 polyps (59%) [95% CI (45.5%, 71.4%)] were more than 5 mm, of these 25 polyps (43%) were between 5 mm–9 mm and 9 polyps (16%) were more than or equal to 10 mm.

**Conclusion:** In this pilot study overall prevalence of adenomas in asymptomatic average risk Afro-Caribbean population in the United States between 50 years and 55 years of age was 21%. 57% of the adenomas were distributed proximally and 59% of the adenomas were larger than 5 mm and 12% of the adenomas were tubulovillous. Although larger cohort is needed this data suggests that it may be necessary to start screening colonoscopy below 50 years of age in Afro-Caribbean patient population similar to the African-Americans.

### Predicting Obstructive Defecation: Symptoms and Physiologic Tests

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**Purpose:** Constipation can be from a variety of disorders including obstructive defecation (OD) and delayed colonic transit. Prior studies have not shown predictive value of symptoms in identifying patients with OD.

**AIM:** To determine which physiologic tests and specific questions of the Rome Pelvic Floor Dyssynergia questionnaire can be used to suggest OD or delayed colonic transit.

**Methods:** A retrospective analysis of patients from May to January 2007 was conducted. Each patient underwent anorectal manometry (ARM), anal electromyography (EMG), balloon expulsion, and whole gut transit scintigraphy. OD was defined by the presence of 2 of the following 3 criteria: 1) inadequate relaxation of the internal anal sphincter (IAS) on ARM; 2) paradoxical increase in EMG activity on bearing down (simulated defecation); 3) inability to expel a 50 cc rectally placed balloon within 3 minutes. The manometric defecation index (DI) was defined as the ratio of intrarectal pressure to external anal sphincter pressure during simulated defecation. Patients were asked questions from the Rome Pelvic Floor Dyssynergia questionnaire: A) straining during movements; B) feeling of incomplete evacuation; C) sen-

sation of blocked stools; D) manual maneuvers to facilitate defecation; E) difficulty relaxing to allow defecation.

**Results:** Of 76 patients, OD was identified in 55 and nonobstructive constipation (NOC) was present in 21 patients. Abnormal DI (<1.2) was present in 47/55 (85%) OD patients and 9/21 (43%) NOC patients. Paradoxical EMG response was present in 38/55 (69%) OD patients and only 1/21 (5%) NOC patients. Abnormal IAS relaxation (<75%) was present in 32/55 (58%) OD patients and 14/21 (67%) NOC patients. Prolonged balloon expulsion (>3 minutes) was present in 16/55 (29%) OD patients and 3/21 (14%) NOC patients. Question A was associated with OD ( $P = 0.054$ ); B was associated with both OD ( $P = 0.035$ ) and with delayed colonic transit ( $P = 0.032$ ); C was associated with OD ( $P = 0.060$ ); D was associated with delayed colonic transit ( $P = 0.056$ ); E was not associated with either OD or delayed colonic transit.

**Conclusion:** The manometric defecation index was sensitive and EMG paradoxical response was specific in identifying patients with obstructive defecation whereas balloon expulsion did not appear to be useful. Questions A (straining during bowel movements) and C (sensation of blocked stools) were associated with obstructive defecation but not delayed colonic transit whereas D (manual maneuvers to facilitate defecation) was associated with delayed colonic transit but not obstructive defecation.

### Is Survival for Rectal Cancer Patients Downstaged to Stage I after Neoadjuvant Radiation Determined by Their Pretreatment Stage? A 10 Year Analysis

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**Purpose:** Owing to the possibility of a more advanced initial stage, rectal cancer patients downstaged to stage I after neoadjuvant radiation may be expected to have a worse prognosis than patients of comparable stage undergoing surgery alone. We compare survival for patients with pathologic stage I rectal cancer after neoadjuvant radiation to stage I patients not receiving preoperative radiation.

**Methods:** Patients who underwent radical resection of the rectum for stage I adenocarcinoma of the rectum between 1988 and 1997 were identified from the prospectively maintained SEER database. Patient and tumor characteristics and survival of patients who underwent preoperative radiation (PRT) were compared with those who did not receive radiation (NRT). The Chi-squared, Fisher's exact and Mann-Whitney tests were used to determine differences between groups as appropriate. The Kaplan-Meier test was used to determine survival and the logrank test to determine significance of difference in survival between groups.  $P < 0.05$  was considered to be statistically significant.

**Results:** 2883 stage I patients (58.2% male) underwent radical resection of the rectum. Tumor grade was well-differentiated (10.5%), moderately differentiated (78.8%), poorly differentiated (10.2%) or undifferentiated (0.5%). 127 patients (4.4%) received preoperative radiation, 176 (6.1%) postoperative and 2571 (89.5%) no radiation. Both RT and NRT groups had similar gender and tumor grade, but RT patients were significantly younger (mean 64 vs 68,  $P < 0.001$ ) than NRT. Median survival was also similar (median 141 vs 144 months,  $P = 0.9$ ). The median number of nodes in the specimen was however significantly lower in PRT than RT (4 vs 7,  $P < 0.05$ ). Patients receiving postoperative RT (PORT) had similar gender ( $P = 0.14$ ), grade ( $P = 0.17$ ) and median survival ( $P = 0.7$ ) compared with PRT. Median number of nodes in PRT was also significantly lower than PORT (4 vs 6,  $P < 0.05$ ).

**Conclusion:** After neoadjuvant radiation, patients with rectal adenocarcinoma downstaged to stage I have a lower lymph node harvest but a comparable median survival to patients not receiving preoperative radiation. Thus such downstaged patients may expect better outcomes determined by their new stage I status rather than the original stage that prompted neoadjuvant therapy.

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### Comparison of Anorectal Manometry to Endoanal Ultrasound in the Evaluation of Fecal Incontinence

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**Purpose:** To compare the results of anorectal manometry (ARM) and endoanal ultrasonography (EAU) in a cohort of patients with fecal incontinence (FI).

**Methods:** Retrospective, single center, descriptive study of 27 patients (20 females) referred to the gastrointestinal motility clinic for evaluation of FI. Patients underwent both ARM to measure anal sphincter function, and EAU to visualize the morphology of the anal canal. Linear regression analysis (Pearson's Correlation Coefficient) was used to correlate findings of ARM and EUS.

**Results:** Mean age of the patients who completed both studies was 56 years (Range 26–87 years). Etiology of FI was obstetric trauma in 4, pelvic surgery in 9, pelvic trauma in 3, pelvic radiation in 1, and idiopathic in 8. Based on the ARM data, 14/27 had a weak external sphincter squeeze pressure and 3 had impaired rectal sensation, while with the EAU there was thinning of the external anal sphincter (EAS) in 3 and complete disruption in 1. IAS thinning was noted in 7/27, scarring of IAS in 2/27 and partial defect of the IAS in 2. Overall only 2/27 had normal findings by combined ARM and EAU. There was no correlation ( $r = 0.48$ ) between EAS function based on ARM and EAS anatomy as assessed by EAU. Similarly IAS function and IAS anatomy did not correlate ( $r = 0.26$ ). However, in the three patients with partial or complete disruption of IAS or EAS on EAU, the ARM showed the corresponding sphincter weakness.

**Conclusion:** 1) In a cohort of middle aged and older patients of both genders seeing a gastroenterologist for varying etiologies of FI, only a small percentage of patients had a normal ARM or EAU. 2) When there are degrees of EAS thinning or partial or complete disruption of the anal sphincters on EAU, a good correlation with ARM is achieved. 3) EAU and ARM are complementary and important investigations for the thorough assessment of the anal sphincter apparatus, which in turn will allow for appropriate management strategies for the majority of patients with FI.

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### Outcomes and Risk Factors for Development of Post-Polypectomy Hemorrhage Requiring Hospitalization

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**Purpose:** To determine the risk factors related to post-polypectomy hemorrhage (PPH) and to determine outcomes of these complications.

**Background:** PPH is a common complication following polypectomy with a reported frequency of 0.3 to 6%. Reported risk factors include polyp size, polyp morphology and patient age.

**Methods:** All outpatients undergoing colonoscopy with polypectomy between January 1, 1999 and April 1, 2007 were included. Data pertaining to the colonoscopy and polypectomy was obtained using the endoscopic database maintained by the Gastroenterology department and analyzed retrospectively. Corporate data store was queried to obtain the list of patients that were admitted to the hospital within 30 days following the colonoscopy. Electronic medical records were reviewed to determine which of these patients were admitted with a diagnosis PPH. Statistical analysis was conducted using chi-square analysis.

**Results:** There were 11,433 patients that had polypectomy performed, of which 36 were admitted due to PPH (0.31%). PPH varied based on the site of polypectomy. PPH was 0.62% following polyp removal from the cecum, 0.56% from ascending colon and 0.92% from hepatic flexure compared to

0% in transverse colon or splenic flexure, 0.27% in descending colon, 0.2% in sigmoid and 0.25% in rectum ( $P = 0.017$  right colon sites compared with transverse and left colon sites). PPH occurred in 0.21% in patients undergoing polypectomy during screening vs 0.43% for other indications ( $P = 0.026$ ). Bleeding occurred more commonly in males 0.47% vs females 0.19% ( $P = 0.003$ ). Size of polyp >10 mm was associated with higher risk of PPH 0.56% vs 0.14% ( $P = 0.013$ ). There was no association with race or type of bowel preparation used. 8 patients were admitted to the ICU. 22/36 (61%) patients required endoscopy for hemostasis and the remainder had spontaneous resolution of bleeding. Mean hospitalization time was 3.7 days.

**Conclusion:** In our study we found that PPH is significantly higher in men. PPH occurs significantly more frequently with polyps greater than 10 mm. PPH appears to occur more frequently with polyps removed from the right colon as compared with those removed from the transverse and left colon. Finally, PPH appears to be more frequent following polypectomy in patients undergoing colonoscopy for a specific indication as compared with those undergoing polypectomy during screening. PPH was easily controlled in most patients with either observation or endoscopic therapy.

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### Complete Resolution of Anemia after Polypectomy of Inflammatory Fibroid Polyp

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**Purpose:** Inflammatory fibroid polyp is an uncommon benign polypoid lesion of the gastrointestinal tract. Inflammatory fibroid polyp is more commonly found in the stomach or small intestine, and rarely in the colon. We present a rare case of an 85 year old female (Jehovah's Witness), presenting with iron deficiency anemia caused by a benign fibroid polyp in the colon.

**Methods:** An 85 year old Hispanic female with a past medical history of HTN, vaginal hysterectomy and family history of colon cancer, was referred to our hospital (a center for bloodless surgery), after being found to have a large colonic polyp in ascending colon and iron deficiency anemia. Her Hg was 10.1, HCT 31.5, MCV 78.2, and her stool for occult blood was positive. On colonoscopy, diverticulosis was seen from descending to sigmoid colon and in the ascending colon a large pedunculated polyp with a very thick stalk was found. At the stalk site 6 cc epinephrine, 1 in 10,000 was injected and the polyp was removed using snare polypectomy. Pathology reported the mass as an inflammatory fibroid polyp with multiple erosions measuring  $4 \times 3 \times 3$  cm in size. An EGD showed mild hiatal hernia, gastric erosions and mild duodenitis. Patient was never given any iron supplements or erythropoietin injections for the anemia. Follow up labs after 10 months demonstrated normal levels of Hb of 14.6 and Hct 41.7.

Thus this patient had an iron deficiency anemia secondary to blood loss from the fibroid polyp which had multiple areas of erosions on its surface, and the anemia resolved on removal of the polyp.

**Conclusion:** Inflammatory fibroid polyp is histologically characterized by a mixture of proliferating fibroblasts and small blood vessels, accompanying a marked eosinophilic infiltrate. The lesion largely affects adults and is more common in the antrum of the stomach, but has occasionally been reported in the small bowel and colon. Although it is generally believed to represent a reactive, nonneoplastic condition, their histogenesis remains unclear. The treatment is surgical excision of the polyp, or colonoscopic resection when it is possible.

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### In Vivo Prediction of Polyp Histology Using High

#### Definition/Magnification and Narrow Band Imaging (NBI)

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**Purpose:** With wide spread use of new generation endoscopes utilizing wide-angle views, high definition (HD)/magnification (Mag) and NBI, en-



doscopists are able to see more diminutive polyps whose clinical significance remains unclear. Chromoendoscopy can differentiate polyp types with high sensitivity but is a cumbersome technique. NBI can be utilized for the same purpose but is less time-consuming. The aim was to predict polyp histology using a combination of white light endoscopy with HD/Mag and NBI.

**Methods:** Prospective evaluation of 100 consecutive patients undergoing screening colonoscopy from Sept 2006–Nov 2006. Olympus H180 colonoscopes were utilized to examine polyps during adequate insufflation using white light/HD/Mag followed by NBI mode. Polyp's histology was then predicted and polypectomies performed. The predicted histology was compared to the true histo-pathological interpretation. The staff endoscopist was modestly familiar with reported patterns visualized under NBI, associated with adenomatous (Ad) or hyperplastic (HP) polyps.

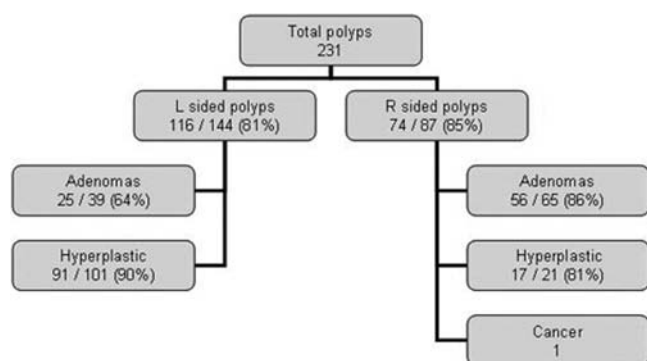
**Results:** Of 231 polyps, 190 (82%) were predicted accurately (Ad = 77%, HP = 89%). A detailed analysis between predicted and true histology of polyps is shown in Table 1.

**Table 1.**

Polyp Characteristics	Agreement 190	Disagreement 40	Accuracy
≤5 mm	154	35	82%
6–9 mm	22	5	82%
≥10 mm	14	1	93%
L sided lesions	116	28	81%
R sided lesions	74	13	85%
Adenomas	81	24	77%
Hyperplastic	108	14	89%
Other: melanosis, leiomyoma, carcinoid, cancer	1 (cancer)	3	
Total distal sigmoid polyps	90	6	93%
Diminutive distal sigmoid polyps	72	3	96%

Figure 1 shows endoscopist's accuracy for histology according to the location and type of polyp. The predicted histological accuracy for HP recto-sigmoid (≤30 cm from anal verge) polyps was 97% and increased to 98.6% for polyps ≤ 3 mm in size.

**Conclusion:** By using a combination of NBI and white light with HD/Mag, we were able to show that polyp histology could be predicted fairly accurately. Up to 99% of the diminutive hyperplastic polyps of recto-sigmoid were identified correctly. This might help to avoid unnecessary polypectomies.[figure1]



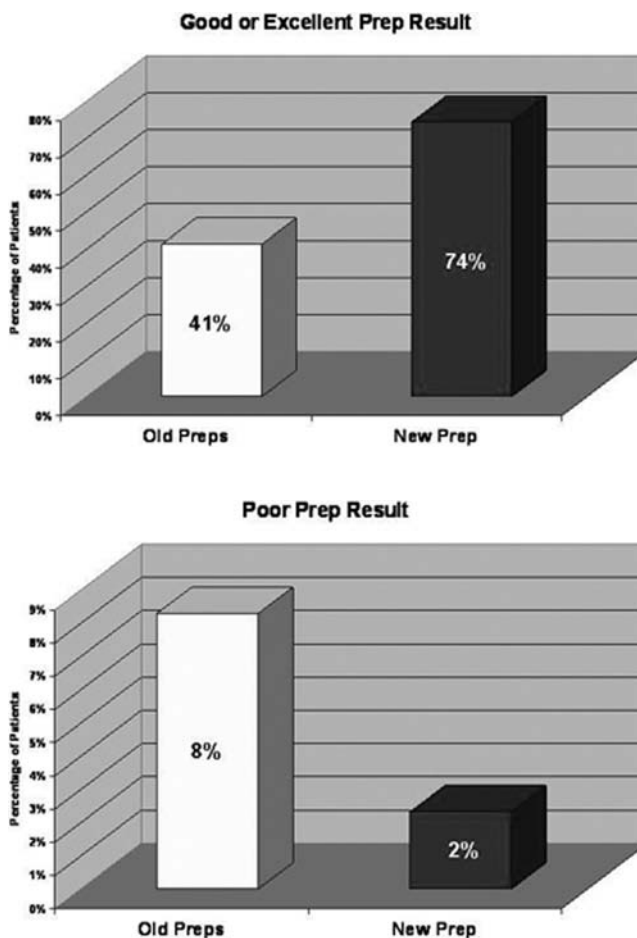
### Addition of Bisacodyl Tabs Dramatically Reduces the Frequency of Poor Colon Preps

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**Purpose:** Poor C-scope preps result in increased complications, costs, and missed cancers. In the past 4 years, despite 4 different 1 and 3-day prep concoctions in 3614 exams, 8% of pts had poor preps. In desperation, we sent out the dove, which returned with an olive branch and 12 tabs of bisacodyl. Our purpose is to determine whether the new C-scope prep 1) improves mucosal visualization and 2) reduces the rate of poor preps.

**Methods:** 100 consecutive pts were prepped by the Nurse Prep clinic in the same manner as the previous 3614 pts, except for the bisacodyl. Pts were instructed to commence on the day before the exam (1) the clear liquid diet, (2) the 12 (5 mg) bisacodyl tabs (3) the gallon of Colyte, (4) the 10 oz of Mag Citrate and (5) liquids for the rest of the day. Pts read either the story of Noah or the Book of Job in the Hebrew Bible and reported to the scope room the next day either by ship or by strips of dry land.

**Results:** There was an immediate and profound improvement in the quality of the colon preps and the behavior of the GI fellows and nursing staff. There was a 33% increase in Good or Excellent preps and a 6% decrease in Poor preps (95% CI = 23.6–42.4,  $P < 0.0001$ ). Age was unrelated to the quality of the prep ( $P = \text{NS}$ ) for all preps. If these results are maintained over the next 30 years, an entire year of professional services will not have been squandered.



**Conclusion:** Addition of 12 bisacodyl tablets (60 mg) to the already nauseating colon prep on the morning prior to the C-scope procedure results in a stunning increase in the frequency of acceptable preps.[figure1][figure2]

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#### Diagnostic Yield of Colonoscopy in Patients Referred with Iron Deficiency Anaemia. Do Patients under 50 Years of Age Merit Such Indication?

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**Purpose:** Iron Deficiency Anaemia (IDA) is one of the common referral indications for patients undergoing colonoscopy. Colonic cancer (5–10%), gastric cancer (5%) and coeliac disease (4–6%) are the most important causes of Iron Deficiency Anaemia, and should be ruled out. British Society of Gastroenterology (BSG) also recommends that all male patients (irrespective of age) and female patients aged 50 or more/ postmenopausal should undergo colonoscopy, besides upper gastrointestinal endoscopy and coeliac screening.

**Methods:** Our aim was to assess the diagnostic yield of colonoscopy in patients referred with iron deficiency anaemia, and to compare the diagnostic yield in patients under 50 years and over 50 years of age. We were specifically looking for cancer pick up rate in the two age groups.

This study was carried out in the light of “Guidelines for the Management of Iron deficiency Anaemia” published by BSG in 2005, which recommends colonoscopy to rule out cancer in addition to above mentioned screening. 147 cases of Iron deficiency anaemia were identified (ferritin <12 ng/ml (females) & <17 ng/ml (males), MCV <80 fl) and were finally included in this study. We collected the data from endoscribe, and patients’ notes were consulted where required. The data was analysed specifically with regards to age. Only those patients who had full colonoscopy done were included in the study.

**Results:** Eighty eight percent (N = 129) were more than 50 years of age and 18 (12%) were less than 50 years of age. 62.5% (N = 92) of patients were female and 37.5% (N = 55) were male. Sixty percent (N = 88) of patients had haemoglobin of less than 9.9 (average 9.6), and 63% (N = 93) had MCV of 60–79 (average 74 fl). 45% (N = 66) had serum ferritin <10 (average 5.7).

In patients aged more than 50, colonoscopy was normal in 39% (N = 51), 26% (N = 33) had diverticular disease, 13% (N = 17) had colonic polyps, 10% (N = 15) had colon cancer, 6% (N = 7) had haemorrhoids, 2% (N = 2) had crohn’s colitis and <1% (N = 1) had angiodysplasia.

However, in patients less than 50 years of age 84% (N = 15) had normal colonoscopy and 16% (N = 3) had polyps.

**Conclusion:** Our study showed that all the cancers were detected in patients more than 50 years of age. Hence, we recommend that colonoscopy should not be a routine investigation for patients of less than 50 years of age presenting with iron deficiency anaemia.

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#### Narrow – Band Imaging for Differentiating Neoplastic and Nonneoplastic Colon Polyps during Colonoscopy in Clinical Practice

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**Purpose:** All polyps are usually removed during colonoscopy, as it is difficult to differentiate between neoplastic polyps (NP) and nonneoplastic polyps (NNP) during standard colonoscopy (SC). Narrow band imaging (NBI) high-

lights the mucosal pit pattern and microvasculature, and may improve the accuracy of distinguishing NP and NNP.

The aim of this study was to evaluate the accuracy of NBI in distinguishing NP and NNP, and feasibility of its use during colonoscopy in clinical practice at an ambulatory surgery center (ASC).

**Methods:** 240 consecutive patients undergoing colonoscopy at an ASC were studied. Duration of colonoscopy with application of NBI during the study period was compared with duration of consecutive colonoscopies performed by the operator from nursing records of previous examinations. Polyps were identified using SC and then imaged with NBI. The polyps were designated as NP and NNP based on SC and NBI. All polyps were resected for histopathology. The sensitivity, specificity, positive and negative predictive values of SC and NBI for differentiating NP and NNP was calculated using histopathology as the reference.

**Results:** 56 subjects 66% male 34% female, mean age of 61.7 years had polyps. Indications were screening colonoscopy 77%, abdominal pain 3.5%, anemia 3.5%, heme positive stool 7%, rectal bleeding 4%, others 5%. 80 polyps were identified and resected. 51 polyps were NP (adenomas) and 29 polyps were NNP (hyperplastic or inflammatory) on pathology. 45/51 NP were correctly identified on NBI compared to 38/51 NP on SC. 28/29 NNP were correctly identified on NBI compared to 24/29 NNP on SC.

The sensitivity for NBI was 88.2% with a specificity of 96.5%, a positive predictive value of 97.8% and a negative predictive value of 82.3%. In comparison SC had a sensitivity of 74.5% with a specificity of 82.7%, a positive predictive value of 88.4% and a negative predictive value of 64.9%. There was no significant difference in the duration of colonoscopy with NBI application (mean 17.5 min vs. 16.4 min,  $P = 0.12$ ).

**Conclusion:** NBI is superior to SC in distinguishing NP and NNP polyps. It can be applied during colonoscopy in a clinical practice setting without a significant increase in the duration of procedure. However, more studies and clinical experience with NBI is required; before it can be used as a standard technique to distinguish NP and NNP during colonoscopy.

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#### Trainees’ Influence on Polyp Detection (TRIPOD). Does Trainee Participation Affect Polyp Detection Rates?

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**Purpose:** Training future endoscopists is essential to meet increasing demands for colonoscopy. Current standards demand a polyp detection rates of 15% in male patients and 25% in females. However, it remains unknown if such criteria are met when trainees are involved during a procedure, or if trainee- participation leads to a substantial delay in procedure time when polyps are found.

**Methods:** We prospectively gathered information about polyp detection rates during open-access colonoscopy (OAC) in a university-based training program. This data was collected as part of a study that aimed to assess patient satisfaction with OAC, whether there was 2nd- or 3rd-year trainee participation or not. As part of a quality improvement initiative, we aimed to assess whether polyp detection rates differed between procedures with or without trainee involvement. As a secondary aim we analyzed procedure times in the two groups. Statistical analysis.

**Results:** 369 patients entered the analysis (181 with trainee participation and 188 without). Most referrals were for screening/surveillance (87%). Attending physicians detected polyps in 31% of patients and 34% of trainee-procedures. In absolute numbers, 96 polyps were detected in the trainee-group versus 94 in the attending group. The number of patients in whom 3 or more polyps, or polyp greater or equal than 1 cm, were detected, was 14 in the trainee group versus 20 in the attending group respectively. On average,

trainee participation during cases with polypectomy delayed the procedure by 8 minutes (42% relative increase).

**Conclusion:** Polyp detection rates do not appear to differ during OAC in our center, whether there was trainee-participation or not, although trainee-participation led to a (tolerable) delay in procedure duration. There was a trend towards finding more polyps or polyps greater than 2 cm in the absence of a trainee, but polyp detection rates were still above national standards when trainees were present. We believe that such analyses will help improve quality of care and training in university training programs.

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### Ischemic Colitis Induced by the Combination of Bisacodyl and Polyethylene Glycol in Preparation for Colonoscopy

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**Purpose:** Laxatives are frequently used in preparation for lower gastrointestinal studies. There have been rare cases of ischemic colitis complicating colonoscopy preparation. We report two patients who developed ischemic colitis immediately following bisacodyl and polyethylene glycol preparation.

**Methods:** The first patient is a 56-year-old man with a history of hypertension and mitral valve prolapse who had an outpatient surveillance colonoscopy. He ingested four tablets of bisacodyl in preparation for his colonoscopy one day before the procedure. After completing the polyethylene glycol preparation, he reported crampy lower abdominal pain. The pain was followed by diarrhea and maroon stool. Colonoscopy revealed an area of patchy submucosal hemorrhage and mucosal edema at the level of the proximal sigmoid colon. Biopsies of the area showed subacute ulceration and fibrosis of lamina propria, consistent with ischemic colitis.

Our second case is a 78 year-old female with a history of hypertension, anemia and osteoarthritis who was admitted to the hospital after an elective colonoscopy. She had ingested her bowel prep the night before which included bisacodyl and polyethylene glycol. After developing abdominal pain, followed by bloody diarrhea, she presented to the hospital. On admission, her abdominal examination revealed lower abdominal tenderness and distension. Abdominal radiograph revealed a pneumoperitoneum. The patient underwent an exploratory laparotomy. Necrotic sigmoid bowel complicated by perforation was identified. A left hemicolectomy was performed. Histology of the resected area demonstrated focal ischemic colitis.

**Conclusion:** Due to its mechanism of action, bisacodyl may result in colonic ischemia by transient reduction in the splanchnic blood flow. When taken in conjunction with a polyethylene glycol purgative, resulting in increased intramural pressure secondary to increased peristalsis, ischemic colitis and perforation may occur. These two cases suggest that careful consideration be given to providing bisacodyl in combination with polyethylene glycol preparations.

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### *Clostridium difficile* Colitis: A Shift from a Traditionally Hospital Acquired Infection to a Community and Nursing Home-Based Disease

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**Purpose:** Until recently, most studies on the incidence and prevalence of *Clostridium difficile*-associated disease (CDAD) have focused entirely on patients hospitalized in the acute care setting. However, CDAD has recently reached epidemic proportions within the general population and within long term care facilities such as nursing homes. This study aims to highlight that the epidemiology of CDAD is shifting from a primarily hospital acquired

disease to an infection arising mostly within our communities and long-term care environments.

**Methods:** This was an IRB-approved retrospective study of hospitalized patients in an inner-city tertiary care hospital in Baltimore, MD. All patients carried the diagnosis of *C. diff* colitis (ICD-9 008.45) between Jan 2000 and Dec 2005. We reviewed 410 hospital medical records to verify the diagnosis of CDAD by ensuring that all included patients had clinical evidence of CDAD with a confirmed positive toxin assay. Patients were then divided into specific categories according to the most likely source of their infection. Categories included *nosocomial*, *nursing home*, *community*, and *other* (i.e assisted living facilities/group homes). The source of infection was considered *nosocomial* if patients developed clinical symptoms of CDAD 48 hours or more after admission with a confirmed positive toxin assay. Those patients with clinical symptoms of CDAD on admission or within 48 hours (with a positive assay) were accordingly divided into their respective categories. Special consideration was given to ensure that all included patients had no previous hospitalizations within the six months prior to diagnosis. Data was acquired using MS Access and analyzed using SPSS.

**Results:** A total of 300 toxin assay positive patients were included in the final analysis. It was found that fifty-three cases (17.7%) were truly *nosocomial*, as compared to eighty-six cases (28.7%) which were *community* acquired, and one-hundred twenty cases (40%) which were *nursing home* acquired. Therefore, two-hundred six cases of CDAD (68.7%) were acquired from a source outside the hospital setting.

**Conclusion:** *Clostridium difficile*-associated disease may be shifting from a traditionally hospital acquired infection to a primarily community and nursing home-based phenomenon. Additional epidemiological studies are needed to further confirm these findings and to develop strategies for limiting the extent of this disease.

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### Assessment of Methane Breath Testing

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**Purpose:** A positive methane breath test has been associated with constipation. Bjornekleit and Jenssen (Scand J Gastro 1982; 17:985) demonstrated the presence of methane in the fasting state and in mid-day sampling (non fasting) in normal volunteers. Le Marchand et al (Environ Health Prospect 1992 Nov; 98:199-202.) demonstrated a clear circadian pattern of excretion for breath hydrogen while methane excretion was constant throughout the day.

**Aim:** To assess change in methane from baseline following lactulose dosing.

**Methods:** One hundred ninety-nine patients were referred to the OFDR gastrointestinal physiology laboratory with chronic lower gastrointestinal complaints for testing for bacteria overgrowth between 8/11/2005 and 6/8/2007. Patients were stratified by baseline methane values: <2 ppm negative, 2-9 ppm low methane producers, >10 ppm high methane producers. Early in our experience, methane breath test was considered complete if the baseline CH<sub>4</sub> was elevated (N = 15) (no lactulose was given and no other samples were taken). The remaining 184 patients were given 10 g lactulose orally. Methane and hydrogen in the exhaled breath was measured every ten or fifteen minutes for three hours using Quintron microlyser.

**Results:** The data is summarized in the table. None of the 149 patients with no measurable methane became positive after lactulose ingestion. When the initial breath was positive for methane, patient could have an increase,

	No CH <sub>3</sub>	Low CH <sub>3</sub>	High CH <sub>3</sub>
Baseline	149	12	38
Fluctuation	0	10	5
Increased	0	0	20
Discontinued*	0	2	13

\* After elevated baseline methane.

decrease, or fluctuation in breath methane. No patients had a decrease in methane during the study. 15 were discontinued as mentioned above.

The above table did not include 3 patients (discontinued because of high H<sub>2</sub>)

**Conclusion:** 1) An initial BT with low positive methane did not show an increase in methane following lactulose;

2) An initial BT with high positive methane increases with lactulose 50% of the time.

3) A negative methane breath test does not become positive after lactulose.

**Conclusion**

1) Lactulose administration has little effect on baseline breath methane values.

2) 25% of our patient population have positive tests for breath methane.

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##### **A Cost Comparison of Metronidazole and Vancomycin in the Treatment of Clostridium Difficile Associated Diarrhea**

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**Purpose:** Clostridium difficile associated diarrhea (CDAD) is currently the leading cause of antibiotic associated diarrhea. Current guidelines recommend metronidazole as the first line therapy due to its low cost. The emergence of more virulent strains and increasing resistance rates of metronidazole have raised questions as to whether vancomycin should be used rather than metronidazole.

**Aim:** To determine whether metronidazole or vancomycin provides the most cost-effective treatment for CDAD.

**Methods:** TreeAge Pro 8.1 software was used to develop a cost comparison model of vancomycin versus metronidazole as first line therapy for CDAD. Separate Markov models were generated to evaluate the drugs' respective cost effectiveness for the treatment of CDAD.

Direct outpatient costs associated with CDAD were obtained from the Medicare database and included clinic visits, antibiotics (metronidazole and vancomycin), and stool tests (Toxin A and toxin B). Direct hospital costs were obtained from the US Medicare DRG's for enteritis/complications.

Monte Carlo simulation was utilized in the comparison models. Patients were assumed to have no greater than 6 recurrences.

**Results:** Using recently reported resistance rates of 20% (metronidazole) and 1% (vancomycin) and a recurrence rate of 20% for each drug, the average treatment cost was \$561 for metronidazole and \$910 for vancomycin. Using probabilistic sensitivity modeling, equivalent costs between the groups were attained only once resistance rates of metronidazole approached 75%. As determined by cost-modeling, vancomycin expense would need to be reduced by 88% to achieve superiority to metronidazole.

**Conclusion:** Despite increasing resistance rates of CDAD to metronidazole, metronidazole outperforms vancomycin as first line therapy in the treatment of CDAD largely due to the expense of vancomycin. First line therapy for CDAD should remain as metronidazole unless resistance rates become substantial or the cost of vancomycin is significantly reduced.

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##### **Is Body Mass Index an Important Marker of Complicated Diverticulitis? A 10 Year Retrospective Review**

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**Purpose:** Obesity is becoming a growing health concern in the general population. The complications of this epidemic affect the endocrine,

cardiovascular and gastrointestinal systems. Multiple studies have linked diverticular disease to obesity. Furthermore, recent research has shown fat to be a critical element in the regulation of immunity and the inflammatory response. In this study, we sought to determine if body mass index (BMI) is associated with a higher incidence of complicated diverticulitis.

**Methods:** A retrospective review of patients hospitalized with complicated diverticulitis between 1997 and 2006 was conducted. Medical, surgical and CT guided interventions were evaluated in reference to age, gender, BMI and length of hospital stay (LOS).

**Results:** Charts of 614 patients hospitalized with complicated diverticulitis were reviewed based on specified inclusion and exclusion criteria. Of those, 36 patients presenting with medically treated diverticulitis with lower gastrointestinal bleed (LGIB) [group 1], 170 patients undergoing surgical intervention for simple diverticulitis [group 2], 50 patients with diverticulitis with abscess [group 3], 64 patients with diverticulitis with peritonitis [group 4], and 41 patients with diverticulitis and CT guided drainage [group 5] were included in this study (N = 325). There was no significant difference between groups by either gender ( $P = 0.066$ ) or BMI ( $P = 0.648$ ). However, there was a difference in the age between groups 1 and 2 ( $P < 0.001$ ), 1 and 4 ( $P < 0.001$ ), 2 and 3 ( $P = 0.014$ ). Furthermore, differences in the LOS were noted between groups 1 and 3 ( $P = 0.001$ ), 1 and 4 ( $P = 0.007$ ), 1 and 5 ( $P = 0.041$ ). No correlation was noted between BMI and LOS in any of the groups (group 1:  $P = 0.061$ , group 2:  $P = 0.650$ , group 3:  $P = 0.485$ , group 4:  $P = 0.813$ , group 5:  $P = 0.679$ ).

**Conclusion:** There has been increasing interest in obesity and its ramifications in all areas of medicine, including diverticular disease. Numerous studies have shown a strong correlation between acute diverticulitis and obesity, particularly in the young population. However, little research has been conducted to conclude what causes complicated diverticular disease and why it happens to a select group of patients. This study was undertaken to identify a possible link between complicated diverticulitis and obesity. Anecdotal reports and few studies have found a parallel association. However, in this retrospective study, no correlation was found between BMI and incidence complicated diverticulitis.

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##### **How Useful Is Digital Rectal Examination in the Diagnosis of Dyssynergia?**

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**Purpose:** In patients with constipation and difficult defecation, anorectal manometry (ARM) is regarded as a gold standard for the diagnosis of dyssynergic defecation. However, it is not widely available and lacks standardization. Digital rectal examination (DRE) may provide vital clues regarding anorectal structure and function that could suggest dyssynergia. However, DRE is not systematically performed, and its clinical utility in the evaluation of dyssynergia is not known.

**Aim:** To examine the diagnostic yield of DRE in pts with constipation and difficult defecation.

**Methods:** Patients presenting to a single gastroenterologist with constipation and difficult defecation (Rome II) were enrolled. All pts completed a constipation questionnaire and had clinical assessment, including a detailed DRE: anocutaneous reflex, resting and squeeze anal sphincter tone, perineal descent, and anal relaxation with straining. A clinical impression of dyssynergia was noted in the chart. Subsequently, all patients had ARM with a solid state, 6-sensor probe. Anal sphincter and intrarectal pressures were analyzed at rest, squeeze and during attempted defecation, and these data were used to identify dyssynergia. A balloon expulsion test (BET) was also performed. The diagnostic yield of DRE was compared with ARM, using manometry as the gold standard.

**Results:** We examined 100 pts (F/M: 94/6, mean age:  $41 \pm 15.3$  yrs) with constipation. Excessive straining, hard stools, incomplete evacuation,  $\leq 3$  BM/wk and use of digital maneuvers were reported by 84%, 88%, 80%, 75% and 40% of patients respectively. Based on DRE (impaired perineal descent or paradoxical anal contraction or impaired push effort), 76 (76%) had dyssynergia. Subsequently, ARM identified 95 pts (95%) with dyssynergia. DRE had as sensitivity of 81% and positive predictive value (PPV) of 99% for diagnosis of dyssynergic defecation. Normal resting tone on DRE had a sensitivity of 81% and PPV of 69% but a weak sphincter had a sensitivity of 25% and PPV of 28%. Normal squeeze tone had a sensitivity of 78% and PPV of 69% whereas a weak squeeze pressure had sensitivity of 31% and PPV of 40%. Anocutaneous reflex was normal in 73%, and absent in 27%. BET had a sensitivity of 49% and PPV of 100%.

**Conclusion:** In patients presenting with constipation in a tertiary care center, DRE has a high sensitivity and PPV in identifying pts with dyssynergic defecation. DRE has good sensitivity and PPV for detecting a normal but not an abnormal resting or squeeze sphincter tone. A prolonged balloon expulsion test is diagnostic but a normal test does not exclude dyssynergia.

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#### Colocutaneous Fistula Causing Diarrhea: A Complication of PEG Tube Replacement

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**Purpose:** Percutaneous endoscopic gastrostomy (PEG) tube placement leading to fistula formation is rare and colocutaneous fistula due to PEG placement has been reported in less than ten cases.

**Case:** A 37 year old male with cerebral palsy and congenital quadriplegia, with PEG tube for enteral nutrition presented with persistent diarrhea of 2 weeks duration leading to hypokalemia and hypernatremia. Stool studies including clostridium difficile toxin, ova and parasites, and cultures were negative. PEG residuals were yellowish and had fecal odor. Further inquiry revealed there was a bedside replacement of PEG tube 2 weeks ago, which coincided with the onset of diarrhea. Gastrograffin through PEG tube and computed axial tomography scan showed the presence of the tube in the transverse colon and an absence of gastrocolic fistula. Diarrhea resolved after discontinuing tube feedings.

**Discussion:** Apart from infection and bleeding, PEG placement can also cause rare complications such as gastrocolic, jejuno-cutaneous and colocutaneous fistulae. These can occur when loop of intestine gets transfixed between the stomach and the abdominal wall during tube placement. Also, these fistulae may remain asymptomatic after initial procedure and become symptomatic only after PEG replacement. Usually dysfunctional PEG tubes are replaced at the bed side without any radiologic or endoscopic guidance and the replaced tube may remain localized in the colon without proper advancement into the stomach.

**Conclusion:** After bedside replacement of the gastrostomy tube, a strong consideration should be given to radiographically confirm the location of the luminal end. Furthermore, recognize colocutaneous fistula as a cause for persistent diarrhea after PEG replacement.

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#### Characterization of Colon Cancer in Patients with Primary Sclerosing Cholangitis and Ulcerative Colitis

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**Purpose:** Little is known about the characteristics of colon cancer in patients with ulcerative colitis (UC) and primary sclerosing cholangitis (PSC). The aims of this study were 1) to describe the histological type, location, and staging of colon cancers and 2) to determine the influence of PSC on tumor characteristic in this population.

**Methods:** A data base identified patients with PSC, UC, and colon cancer evaluated at Mayo Clinic Rochester (1995–2005). Records were reviewed for demographics, age at diagnosis of colon cancer, PSC, and UC; and histological grade and location of colon cancer.

**Results:** Twenty-nine patients with UC and PSC developed colon cancer with a mean age (standard deviation) of 50.6 (10.6) years (range, 28–83 years) and 69% were male. Thirteen (45%) patients had a history of PSC before the diagnosis of colon cancer with a median duration of 44.5 months (range, 1–105 months), while the remaining 16 patients had colon cancer diagnosed at the same time or prior to the diagnosis of PSC with a median duration of 1 month (range, 0–57 months). Of the 24 patients who had histological grading, 17 patients had quiescent to mildly active UC, while only 7 patients had moderate to severely active UC at the time of the diagnosis of colon cancer. All of the colon cancers were adenocarcinomas. The majority (90%) of the cancers were histological grades 2–3 (out of 4). According to TNM staging system for colon cancer, 10 patients had stage I cancer, 6 had stage II, 7 had stage III, and 5 had stage IV cancer. Twenty cancers (69%) were located on the right side of the colon defined as ileocecal valve to the splenic flexion. The tumor characteristic among patients who had PSC diagnosed prior to the diagnosis of colon cancer did not differ from those patients who developed colon cancer prior or synchronous to the diagnosis of PSC with regard to age at the time of diagnosis of colon cancer, gender, activity of UC, tumor grading and staging, and location of the tumor.

**Conclusion:** Colon cancer was more likely to develop in the right-sided colon in young individuals with UC and PSC. The development of PSC has no impact on the characteristic of colon cancer. This information may be important in decision making for colon cancer surveillance in this population. Surprisingly, many cases of PSC were not recognized until after the colon cancer was found which may suggest a need for more aggressive screening for PSC in patients with UC.

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#### Elevated HbA1c Is an Independent Predictor of Aggressive Clinical Behavior in Patients with Adenomatous Colonic Polyps

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**Purpose:** To determine if poor control of DM is associated with increased prevalence of colonic adenomatous polyps (AP), especially advanced AP.

**Methods:** We performed a retrospective review of 652 patients with DM-2 and AP. HbA1c levels were evaluated as in index of glycemic control over the year that preceded diagnosis of AP. 40 factors were assessed in patients grouped into well controlled ( $\text{HbA1c} < 7.5\%$ ) & poorly controlled DM ( $\text{HbA1c} \geq 7.5\%$ ). Factors in each group were examined by univariate analysis and logistic regression analysis to determine independent predictors of aggressive AP behavior.

**Results:** Our results are summarized in table 1. Logistic regression showed that patients with  $\text{HbA1c} \geq 7.5$  presented with more advanced AP, greater right sided AP and a greater number of AP. Patients using NSAIDS had a lesser incidence of advanced AP ( $P < 0.01$ ). Concurrent use of insulin and NSAIDS appeared to negate any protective effect of NSAIDS.

**Conclusion:** Poor glycemic control in patients with DM-2 independently predicts a clinical aggressive course for patients with AP. Small differences in HbA1c elevation may lead to variations in the behavior of AP.

Table 1.

Univariate Analysis				
	Normal HbA1c (N = 339)	Elevated HbA1c (N = 313)	O.R. (95% CI)	P
Present with Advanced Adenomatous Polyp, (%)	13.2	31.2	6.2 (2.4–15.5)	>0.005*
Right Sided Adenomatous Polyp, (%)	15.4	32.9	5.6 (2.2–13.7)	0.001*
Mean Age at Diagnosis of Adenomatous Polyp	67.8 (52–81)	64.1 (51–76)	–	0.001*
Mean Polyp size, (mm)	6.7 (3–20)	10 (4–30)	–	0.001*
Mean Polyp Number	2.5 (1–7)	5.5 (2–20)	–	>0.005
Smoker, (%)	42.6	60.5	2.1 (0.89–4.79)	0.05*
Multivariate Logistic Regression Analysis				
DEPENDENT VARIABLES			95% CI	P
AP site (Right side = 1)			0.04–0.07	0.69
Polyp Number			0.01–0.15	0.03 *
Age at Diagnosis			-0.06–0.01	0.21
Smoker			-0.14–0.84	0.16
Right Sided Polyps			0.06–1.04	0.03 *
Advanced Polyps			0.21–1.36	0.007 *

\*Statistically significant

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**Simultaneous Assessment of Colonic Transit Using Wireless Capsule (SmartPill®) and Radiopaque Markers in Healthy Subjects and Effects of Gender**

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**Purpose:** Colonic transit time (CTT) is used in the evaluation of constipation. Conventionally, CTT is assessed by ingesting radiopaque markers (Sitzmarks® (SZ) followed by abdominal x-ray(s). However, there is limited normative data, gender effects are unclear, and the technique is hampered by poor compliance and complex protocols. Recently, the SmartPill® (SP) wireless pH and pressure recording capsule has been advocated for assessing CTT. The **aim** of this multicenter study was to simultaneously assess and compare CTT as measured by SP with that of SZ in healthy subjects and to assess the effects of gender.

**Methods:** After overnight fast, subjects ingested a nutrient bar (260 kcal) followed by a SZ capsule (24 markers) and a SP capsule. Subjects were instructed to wear a data receiver for 5 days or until SP was expelled and to record their bowel habit on a stool diary. Abdominal x-rays were obtained on day 2 and day 5. SP tracing was examined to assess gastric emptying time (GET) (time to sudden rise in pH >4), small bowel transit time (SBTT) (time to cecal entry with >1 pH drop after GET), CTT (time from cecal entry to abrupt temp. drop), and whole gut transit time (WGTT) (time from ingestion to abrupt temp. drop). The number of retained markers, transit times, and gender differences were assessed and compared.

**Results:** Table (mean ± SEM, \* =  $P < 0.05$ ). 70 (36 M (mean age = 25 yrs)/34 F (mean age = 38 yrs), mean age = 37 yrs) were studied. The SP CTT correlated with % of markers expelled on day 2 ( $r = 0.72$ ,  $P < 0.001$ ) and on day 5 ( $r = 0.54$ ,  $P < 0.001$ ). The number of markers retained on Day 5 were greater ( $P < 0.001$ ) in females and likewise, the SP CTT was also slower ( $P < 0.03$ ) when compared to males. The GET ( $P < 0.002$ ) and WGTT ( $P < 0.03$ ) were also slower in females. All subjects expelled the SP.

**Conclusion:** This large prospective study demonstrates very good correlation of colonic transit as measured by SmartPill® with conventional SZ technique. Also, women had slower gut transit time when compared to men. Thus, gender should be considered when interpreting CTT measurements. SP is a valid technique of measuring colonic and regional gut transit time.

	# Markers Day 2	# Markers Day 5	GET	SBRT	CTT	WGTT
Whole Group	8.9 ± 1.0	1.1 ± 0.4	3.6 ± 0.3	3.8 ± 0.2	29 ± 3	37 ± 3
Females	11.2 ± 1.5	1.7 ± 0.8	4.1 ± 0.5	4.0 ± 0.3	35 ± 5	43 ± 5
Males	6.6 ± 1.3	0.4 ± 0.2*	3.2 ± 0.3*	3.6 ± 0.2	23 ± 3*	31 ± 3*

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**Safety of Colonoscopy during Pregnancy**

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**Purpose:** Whereas colonoscopy is relatively safe in the general population, the safety of colonoscopy during pregnancy is inadequately studied with only 15 reported cases. The safety of colonoscopy during pregnancy involves the unique issue of fetal safety. We analyze the fetal safety of colonoscopy in 23 pregnant patients.

**Results:** 23 patients (8 primigravida, 15 multigravida) underwent colonoscopy during pregnancy from 1986 through 2006 at William Beaumont Hospitals. Their mean age was 29.7 ± 4.7 years (range 20–38 years). Mean gestational age at colonoscopy was 17.9 ± 7.8 weeks (range 2–33 weeks). 4 patients had colonoscopy during 1st trimester, 16 in 2nd trimester and 3 in 3rd trimester (13 as inpatients). Colonic preps included: oral sodium phosphate in 5 patients, sodium phosphate enema in 4, magnesium citrate in 3, polyethylene glycol in 4 and other in 5 (no prep in 1). Anesthetic agents included meperidine (N = 7), fentanyl (N = 6), thiopental (N = 4), midazolam (N = 2), morphine sulfate (N = 2), and other in 3 (unsedated in 6). Mean duration of endoscopy was 19.4 ± 10.3 min (range 8–45). The procedure was well tolerated in 78%. Primary indications for colonoscopy: hematochezia in 10, diarrhea in 4, foreign body in 1, and other in 8. Major new findings/therapy included: new ulcerative colitis in 3, hemorrhoids in 3, ischemic colitis in 3, established IBD in 2, foreign body removal in 1, new Crohn's in 1, and other in 4 (normal colonoscopy in 6). The cecum was reached in 14, transverse colon in 6, hepatic flexure in 2, and near splenic flexure in 1 pt. Three patients underwent snare polypectomy, and 2 had hot biopsy. Patients were hospitalized for 2.6 ± 4.7 days (range 0–20) after index colonoscopy. Maternal colonoscopy complications include hypotension in 3 and minor symptoms in 6. Two patients had spontaneous abortions (both in 1st trimester; 5 days and 5 weeks after colonoscopy). All other infants were delivered alive with no congenital malformations noted in the infant nursery. Mean age of gestation at delivery was 37.8 wks ± 2.2 (N = 19,

range 33–40). Mean APGAR score at 1 min was  $8.1 \pm 1.0$  ( $N = 20$ , range 5–9), and at 5 min was  $9.0 \pm 0.3$  ( $N = 19$ , range 8–9), birth weight  $3.1 \pm 0.6$  Kg ( $N = 19$ , range 1.9–4.2). Fetal outcomes ( $N = 19$ ) included low birth weight ( $< 2500$  grams) in 2 infants, twin gestation in 1 and premature delivery ( $< 37$  wks) in 9.

**Conclusion:** Colonoscopy appears to be relatively safe and can be performed when strongly indicated in the 2nd and 3rd trimesters of pregnancy.

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### Post-Surgical *Clostridium difficile* Infection

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**Purpose:** *C. difficile* is the most common nosocomial infection and *C. difficile* colitis (CDC) is a frequent cause of morbidity and mortality among hospitalized patients. Although CDC has been studied extensively in medical patients, the incidence of this infection and this disease hardly has been investigated in surgical patients. The aims of this study were to identify the pre-operative risk factors associated with development of post-operative CDC, and to determine if any predisposing factors were associated with mortality from this disease.

**Methods:** We constructed a cohort of all in-patients in 2006 who had undergone surgery involving the stomach, small bowel, colon, appendix, anorectum, gallbladder and biliary tract, pancreas, hernia repair or non-otherwise specified (NOS) abdominal surgery. We performed a retrospective review of the charts of all patients who had a *C. difficile* toxin assay post-operatively.

**Results:** We identified 1214 patients who had undergone one of the specified surgeries (422 M; 792 F). 45 patients (4%) were found to have at least one positive *C. difficile* toxin assay post-operatively. The mean age of the study population was 57.6 yrs ( $\pm 19.4$  yrs) for all patients, 63.8 yrs ( $\pm 17.7$  yrs) for those suspected to have CDC, and 67.2 yrs ( $\pm 17.1$  yrs) for those with a positive toxin assay.

Pre-operative factors associated with post-operative toxin positivity were age (OR 1.34 for each 10-year increment in age; 95% CI 1.13–1.60); male gender (OR 1.84; 95% CI 1.01–3.34); proton pump inhibitor (PPI) use within 10 days of surgery (OR 2.00; 95% CI 1.08–3.71;  $P$ -value 0.03); antibiotic use within 30 days of surgery (OR 2.04; 95% CI 1.11–3.77); length of hospitalization prior to surgery (OR 1.58 for every 5 days of hospitalization; 95% CI 1.30–1.93); and a low serum albumin level on admission (OR 2.00 for each loss of 1 g/dl, 95% CI 1.32–3.03).

Two pre-operative factors were associated with post-operative mortality from CDC: a low serum albumin level on admission (Hazard Ratio (HR) 3.41 for each loss of 1 g/dl; 95% CI 2.59–4.49); and a high serum creatinine on admission (HR 1.55 for each increment of 1 mg/dl; CI 1.02–2.22).

**Conclusion:** Post-surgical CDC is a significant complication of “abdominal” surgery that needs to be addressed carefully. Age, male gender, PPI use, antibiotic use, length of hospitalization, and low serum albumin levels are important risk factors in the development of post-surgical CDC. High serum creatinine and low serum albumin levels are associated with higher mortality rates.

## CLINICAL VIGNETTES

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### Symptomatic Mallory-Weiss Tear – A Rare Complication of Peroral Colon Lavage Preparation

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**Purpose:** To describe a rare symptomatic complication of peroral colon lavage preparation.

**Methods:** Colonoscopy is now frequently performed as a primary colorectal cancer screening modality. I recently cared for a patient who sus-

tained a rare complication “associated” with the performance of screening colonoscopy.

**Results:** A 72 year-old, average-risk patient presented for direct-access screening colonoscopy. Upon pre-procedure questioning, the patient mentioned that she had difficulty ingesting the colon lavage preparation, which included magnesium citrate, bisacodyl, and polyethylene glycol solution. Non-bloody vomiting occurred 12 hours prior to the procedure. The patient volunteered that the rectal effluent turned from yellow to blackish in color, during the night before which the procedure was performed. She was taking an NSAID intermittently, but this practice was discontinued 5 days prior to presenting for the procedure. There was no recent iron or bismuth ingestion. Physical examination showed slightly pale conjunctivae, but was otherwise unremarkable. We discussed also performing upper GI endoscopy, should it be deemed appropriate upon completing the colonoscopy. The patient was agreeable, and informed consent was obtained for both procedures.

The colonoscopy was performed under moderate sedation. The examination was completed to the cecum and the mucosa was coated with melanic residue (which was suctioned and tested overtly positive for blood). The terminal ileal mucosa was similarly coated with black, bloody residue. The colonoscopy was otherwise normal (within the limits of the suboptimal preparation). Given these findings, upper GI endoscopy was then performed.

At upper GI endoscopy, a prominent 3 cm nonbleeding Mallory-Weiss tear was found at the EG junction. No endoscopic therapy was deemed necessary, and she was discharged home on a proton-pump inhibitor (4 week course), with instructions to avoid ASA/NSAID use for 4 weeks. A CBC revealed a Hgb of 10.7 g% (in contrast to a value of 13.8 g%, upon routine blood testing which had been performed 3 months earlier). The patient recovered uneventfully.

**Conclusion:** This case highlights a potential, albeit rare complication, which can be seen in association with peroral colon lavage preparation, which was administered prior to screening colonoscopy. Given that screening colonoscopy is now frequently performed, and nausea and vomiting are not a rare occurrence during the preparation, it is possible that such symptomatic events may occur with increasing frequency in the future.

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### “Kissing” Patches-An Uncommon Appearance of Cervical Esophageal Heterotopic Gastric Mucosa

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**Purpose:** To describe an uncommon appearance of heterotopic gastric mucosa (HGM) in the cervical esophagus.

**Methods:** An “inlet patch” refers to a small (usually  $\sim 0.5$  to 2 cm) island of red, velvety heterotopic gastric mucosa, which is often conspicuous when viewed amid the more pink-colored normal esophageal squamous mucosa. These “patches” are usually found in the cervical esophagus, immediately below the upper esophageal sphincter. HGM may be found in  $\sim 10\%$  or more of patients, when the cervical esophageal region is carefully examined.

**Results:** Over the years, I have found many patients who have had cervical esophageal HGM, which endoscopically appeared as 2 “kissing” patches, noted at opposite sides of the lumen. One such case is shown in Figure 1. I have found that in patients with cervical esophageal HGM, the solitary island of gastric tissue is most commonly noted at the 7 to 8 o’clock position (which corresponds to the posterior position). In those in whom I’ve found “kissing” islands of cervical esophageal HGM, the “accessory” patch is usually smaller and visualized in the 1 to 2 o’clock position (which corresponds to the anterior position). I would anecdotally estimate cervical esophageal HGM to have this less common appearance in  $\sim 5\%$  of cases in whom cervical esophageal HGM is detected.

**Conclusion:** Cervical esophageal HGM can uncommonly present endoscopically as 2 “kissing” patches, located on opposite sides of the esophageal lumen.[figure1]



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#### Massive Bilateral Hepatic Hydrothoraces with Minimal Ascites

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**Purpose:** To describe an uncommon presentation of hepatic hydrothorax.

**Methods:** A 77 yo male presented with recurrent massive bilateral pleural effusions. Background medical history included systemic hypertension, atrial fibrillation and a remote history of colon carcinoma. He was initially evaluated by my associate 9 months earlier, when abnormal liver biochemical tests were noted. At that time, he had hyperalkaline phosphatemia ( $5 \times$  ULN). The serum transaminases were "trivially elevated" ( $<2 \times$  ULN). The serum total bilirubin was normal and the albumin was mildly depressed at 3.1 g/dl. Full serologic/virologic hepatic investigation was normal aside from the alpha-1-antitrypsin phenotype revealing MS Pi-type heterozygosity. AMA was specifically negative. An ERCP was performed, which revealed "pruning" of the intrahepatic biliary radicals, most consistent with underlying cirrhosis (as opposed to PSC). Liver biopsy revealed "bland" bridging fibrosis. He had no ascites at the time and was to be followed expectantly. He then presented with massive, symptomatic bilateral pleural effusions. He underwent multiple thoracenteses, which showed "transudative" fluid. Pleuroscopy showed no abnormality, and echocardiography was normal. Consultation was then requested after pleurodesis failed to alleviate the problem.

**Results:** During this evaluation, abdominal CT revealed a "scalloped" liver edge and no appreciable ascites. Ultrasound-guided diagnostic paracentesis of a 2 cm RLQ fluid collection confirmed a portal-hypertensive fluid (SAAG = 1.6 g/dl). Doppler interrogation of the portal and hepatic venous systems revealed no thrombosis. Radionuclide scanning was performed after 6.2 mCi of TC99m macroaggregated albumin was injected into the peritoneal cavity (right lower quadrant). This confirmed prompt tracer localization (at 40 min) into both pleural spaces, and a left-sided chest tube, which was in place at the time. Vigorous sodium restriction and combination diuretic therapy were unsuccessful in controlling the pleural fluid accumulation. The patient underwent TIPS placement, which alleviated his bilateral hepatic hydrothoraces.

**Conclusion:** This case highlights an uncommon presentation of hepatic hydrothorax, where pleural fluid accumulation was both bilateral and occurred

in the absence of significant ascites. Radionuclide instillation into the peritoneal cavity was employed to facilitate the diagnosis, and TIPS placement successfully alleviated the symptomatic pleural effusions.

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#### "Mark and Clip" in Difficult Cases of Gastrointestinal Hemorrhage

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**Purpose:** To describe the use of "mark and clip" method, employed in a case of recurrent GI hemorrhage.

**Methods:** An 89 yo patient presented with low-volume hematochezia. Background history included diverticulosis and she ingested no ASA/NSAID or anticoagulants. Upon presentation, Hb was 14 g%, she was hemodynamically stable and no further bleeding occurred over 48 hrs. The patient desired no evaluation, and immediately prior to planned hospital discharge, large volume, bright-red colored, painless hematochezia recurred. On this occasion, she became transiently hypotensive and the Hb fell to 6 g%. A bleeding scan suggested active bleeding from the left colon. EGD was normal. At colonoscopy, pancolonic diverticulosis was noted, but no active bleeding was seen, and ileal intubation was normal. A large adherent clot was seen in the mid-sigmoid. The clot was flushed away and a small-neck diverticulum was noted beneath. A tiny erosion was noted at the neck of the diverticulum, but no visible vessel could be seen. Epinephrine solution was injected at the neck of the diverticulum and the site was marked with ink, as it was thought to be a potential source of bleeding. Bleeding recurred 48 hours later with recurrent transient hypotension. Repeat colonoscopy again revealed no active bleeding and no clot was seen in the sigmoid region. A metal clip was placed in the region of the previously placed ink mark, for possible radiologic identification of this area of presumed hemorrhage. Hemodynamically significant bleeding recurred another 36 hours later, and mesenteric angiography was requested.

**Results:** At angiography, no bleeding site was initially seen on either the SMA or IMA "runs." The radiologist then performed a selective contrast injection in the region of the "sigmoid clip" (IMA distribution) and rapid extravasation was noted. Hemorrhage was arrested with a third-order "super-selective" embolization. Bleeding has not recurred after a 10 month period.

**Conclusion:** In cases of recurrent, "stuttering" gastrointestinal hemorrhage, one should consider the use of both endoscopic mucosal marking and simultaneous clip placement. The former can be used to facilitate identification during repeat endoscopy or surgery, and the latter can be beneficial during angiographic investigation. Due to their expense, these maneuvers should not be employed routinely, but rather as an adjunct under special circumstances (e.g. cases of diverticular hemorrhage, Dieulafoy bleeding) where potential bleeding sites may be difficult to re-identify, if repeat intervention is required.

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#### Refractory and Coexistent Crohn's Disease with ITP: A Clinical Dilemma

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**Purpose:** To describe a novel approach utilized in a case of refractory, co-existent Crohn's disease and idiopathic thrombocytopenic purpura (ITP).

**Methods:** Case Report: 58 yo female was hospitalized with bloody diarrhea and severe thrombocytopenia. Crohn's disease spanned 2 decades and she had previously undergone a partial colon resection. She was hospitalized on two recent occasions and was cared for by another gastroenterologist. Recent colonoscopy (done when the platelet count was 242,000/ul), revealed changes of severe Crohn's colitis. She was glucocorticoid-dependent (50 mg of prednisone daily). She had reported questionable allergies/intolerances to all 5-aminosalicylate preparations, 6MP, methotrexate, and metronidazole.



Diffuse urticaria occurred after (4) infliximab infusions (despite an excellent clinical response, and administration of a “pre-treatment” protocol). ITP (diagnosed 10 years ago) progressed and did not respond to glucocorticoids, splenectomy, rituximab, cyclophosphamide and other therapies. She was seen at a tertiary referral center for opinions from the IBD and hematologic perspectives. No novel approach was recommended, and a surgical team considered treatment of her IBD contraindicated (platelet count now ~4,000/ul, despite platelet transfusions). I was asked to see the patient after transfer back to our community hospital. She was having 12 bloody bowel actions daily.

**Results:** The platelet count remained ~ 4,000/ul. After discussion, I recommended a trial of oral 5-aminosalicylate, and budesonide was started, in anticipation of tapering of prednisone. Given prior response to infliximab, (but severe allergic reaction), a humanized anti-TNF monoclonal antibody was started (adalimumab 160 mg sc at time 0, 80 mg sc at week 2, then 40 mg sc at week 4, and every 2 weeks, thereafter). All the above interventions were tolerated and diarrhea improved. Six weeks later, she was discharged, having 5 soft, non-bloody bowel actions per day. Twelve weeks after starting adalimumab, prednisone was withdrawn. From the IBD perspective, she remains in clinical remission after 4 months.

**Conclusion:** Transition to adalimumab was successful in achieving and maintaining clinical remission with simultaneous, treatment-refractory Crohn's disease and ITP, with previously demonstrated severe allergy to infliximab. The ITP remained untreatable, and this limited the ability to utilize more traditional medical (6MP, MTX) and surgical therapies for the underlying IBD. Adalimumab “salvage therapy” was successful in this desperate clinical situation.

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#### “Delayed” Sustained Virologic Response after Treatment of Hepatitis C with Pegylated Interferon and Ribavirin

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**Purpose:** To describe a case of “delayed” sustained virologic response (SVR) after treatment of chronic hepatitis C virus (HCV) infection with pegylated interferon (PEG-IFN) and ribavirin (RBV).

An otherwise healthy 36 yo male presented for evaluation of chronic HCV infection in 10/00. Evaluation revealed mild hyperaminotransferasemia and low-titer (178,654 IU/ml), type 1b viremia. Pre-treatment liver biopsy revealed A3/F3 disease. Treatment with PEG-IFN alpha-2b (150 mcg subcutaneous weekly) in combination with RBV (1000 mg orally daily, in divided doses) ensued, with regular hematological, biochemical and clinical monitoring. Serum aminotransferases rapidly normalized, and remained within normal limits. In 6/01, after 24 weeks of combined antiviral therapy, the HCV level, however, remained positive at >600,000 IU/ml, by quantitative PCR analysis. Given this, the patient was characterized as being a non-responder, and the combination antiviral therapy was withdrawn. The patient was to be followed clinically, and as he was planning to move, he was to establish care with another hepatologist in the Midwestern US.

The patient re-presented in 1/07, after moving back to upstate NY. At that time, he mentioned that evaluation in Iowa, where he had transiently lived, suggested that he no longer had evidence of HCV infection. In the interim, he received no other antiviral therapy, and took no herbal, prescribed or OTC medications. There were no other previous or intercurrent medical illnesses. Records were obtained for review, and these corroborated that in 10/03, HCV was undetectable by quantitative PCR (lower limit of detection = 200 IU/ml). HCV quantitative PCR was also negative in 1/07 and 2/07. HCV qualitative PCR was also negative in 3/07 (lower limit of detection = 50 IU/ml). The liver biochemical test profile also remained within normal limits. “Delayed” SVR was ultimately noted to occur in this unusual case, despite there being firm documentation of a lack of virologic response while on combination PEG-IFN/RBV for a duration of 24 weeks. “Spontaneous” viral clearance unrelated to the previous antiviral therapy remains a possibility. This case highlights an unusual course of sustained HCV clearance, after

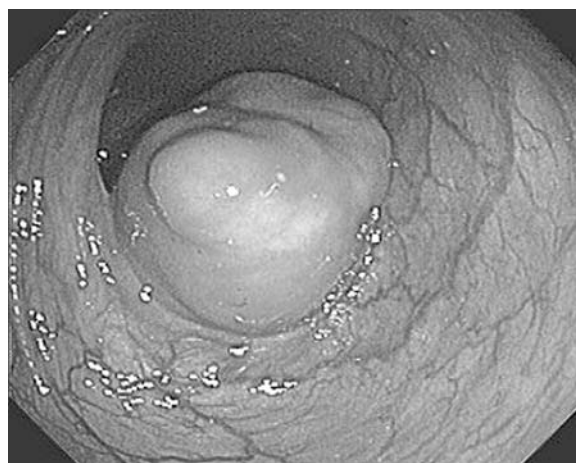
what was initially documented to be unsuccessful combination interferon-based antiviral therapy.

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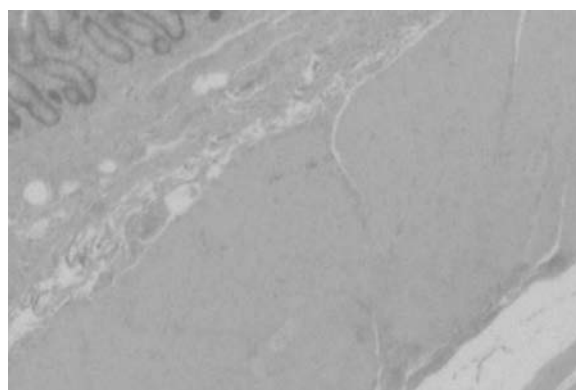
#### Atypical “Intramuscular” Colon Lipoma

Kevin J. Herlihy, MD, FACP, Jayant R. Paranjpe, MD, FCAP, Joseph C. Yarze, MD, FACP, FACP, FASGE\*. GI Division, Gastroenterology Associates of Northern New York, Glens Falls, NY and Department of Pathology, Glens Falls Hospital, Glens Falls, NY.

**Purpose:** A 51 yo male presented for screening colonoscopy. The exam revealed an ~ 4 cm subepithelial mass in the distal transverse colon region.[figure1] The lesion was diffusely firm to palpation with closed biopsy forceps, and a “cushion sign” was unable to be demonstrated. The lesion was lobulated and endoscopic biopsies revealed only hyperplastic tissue. An abdominal CT demonstrated the lesion to be hypodense, measuring -113 Hounsfield units. The CT radiographic findings suggested the lesion to be a lipoma. One section of the CT scan, however, suggested a non-lipomatous, soft-tissue rim of unclear significance. The patient offered that he had been experiencing vague left upper quadrant distress. Options of expectant management, EUS and surgical resection were discussed. Given that the lesion displayed some characteristics atypical for a lipoma, he opted for surgical resection.



Laparoscopic transverse colon resection proceeded uneventfully. Histopathology revealed the lesion to be a lipoma, which was within the muscularis propria layer. [figure2] The unusual histopathology of this lipoma accounted for multiple unique aspects of this case. It is decidedly unusual for a lipoma to be diffusely firm to palpation by biopsy



forceps. Also, by CT scan, this lesion appeared to have a soft tissue rim along its border. These findings are likely accounted for by the fact that histopathology revealed the lipoma to be within the muscularis propria. This histopathologic finding may also have contributed to this lipoma's lobulated appearance.

Colon lipomas can occasionally be associated with atypical colonoscopic and radiographic features. In this case, such atypical findings were likely related to the lipomatous lesion being within the muscularis propria, as opposed to the submucosal layer.

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### Systemic Mastocytosis: A Rare Cause of Portal Hypertension

*Seth Sweetser, MD, Patrick S. Kamath, MD\*. Division of Gastroenterology and Hepatology, Mayo Clinic College of Medicine, Rochester, MN.*

**Purpose:** We present a rare case of systemic mastocytosis masquerading as advanced liver disease. An 80-year-old Caucasian man was referred for evaluation of ascites and esophageal varices. His history was notable for frequent watery stools occurring on a daily basis and a thirty pound weight loss over the past year that had remained undiagnosed despite an extensive work-up. In the interim, he had been diagnosed with chronic liver disease of unclear etiology based on the presence of esophageal varices, ascites, and hypersplenism. He reported intermittent abdominal cramping but denied fever, night sweats, rashes, itching, or flushing. On exam, he appeared cachectic and his abdomen was distended with shifting dullness. An abdomen/pelvis CT showed hepatosplenomegaly, ascites, and punctate sclerotic bone lesions. Labs were significant for WBC  $5.5 \times 10^9/L$  with 49% monocytes, hemoglobin 11 g/dL, platelets  $93 \times 10^9/L$ , ALT 111 U/L, AST 67 U/L, alkaline phosphatase 601 U/L, total bilirubin 0.9 mg/dL, and INR of 3.3. Ascitic fluid analysis showed a SAAG of 2.6, total protein of 1.6 g/dL, and 350 cells with 88% monocytes. Gram stain, bacterial culture, and cytology of the ascitic fluid were negative. Liver biopsy revealed nodular regenerative hyperplasia. A bone marrow exam was hypercellular with 20% involvement by systemic mastocytosis. Tryptase immunostaining of the liver biopsy revealed mast cells within the portal areas. Additionally, a serum tryptase was 243 ng/dL (nl <11.5) which confirmed the diagnosis.

**Conclusion:** Systemic mastocytosis is a rare cause of portal hypertension. Possible mechanisms of portal hypertension in mast cell disease include increased blood flow in the splenic vein, splenic arteriovenous shunting secondary to histamine release, increased intrahepatic resistance secondary to mast cell infiltration, and nodular regenerative hyperplasia. In this case, portal hypertension was likely caused by nodular regenerative hyperplasia and infiltration of portal areas by mast cells. The diagnosis of systemic mastocytosis was considered only after realizing that the diarrhea could not be explained by the degree of portal hypertension and noting the presence of sclerotic bone lesions which prompted a bone marrow biopsy and tryptase measurement. This case highlights the fact that systemic mastocytosis should be considered in the differential of causes of portal hypertension in individuals with evidence of advanced liver disease even when the characteristic cutaneous manifestations of mast cell disease are absent.

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### A Broken Heart from Pancreatitis

*Joseph Y. Chang, MD, MPH\*, Gautam Kumar, MBBS. Mayo Clinic College of Medicine, Rochester, MN.*

**Purpose:** An 83-year-old female presented with a two day history of nausea, vomiting, and epigastric pain. Initial evaluation was consistent with acute pancreatitis with lipase of 1064 U/L, amylase 1271 U/L; with normal transaminases, total and direct bilirubins, and alkaline phosphatase. Abdominal ultrasound was negative for gallstones but showed a dilated common bile duct at 11 mm. She underwent endoscopic retrograde cholangiopan-

creatography with lateral sphincterotomy and placement of pancreatic duct stent. Due to poor clinical progress, she later underwent computed tomography of the abdomen, with findings consistent with severe pancreatitis. She subsequently developed retrosternal chest pain, dyspnea, diaphoresis and hemodynamic instability. Electrocardiogram showed new left axis deviation, intraventricular conduction delay and anteroseptal ST elevation. Cardiac biomarkers were elevated with troponin-T of 0.52 and CK-MB of 24.6. Transthoracic echocardiogram (TTE) demonstrated reduced ejection fraction at 20%, with new diffuse regional wall motion abnormalities. Management for presumed myocardial infarction with aspirin, beta-blocker therapy, and anticoagulation with unfractionated heparin was started and she was sent for emergent cardiac catheterization. However, no flow restricting lesions were found and left ventriculography reported akinesis of the apical septal, posterolateral, anterolateral, apical and diaphragmatic segments; findings consistent with the diagnosis of cardiogenic shock secondary to transient left ventricular apical ballooning, also known as "broken heart syndrome". Following this event, the patient had a protracted hospital course requiring almost 60 days of hospitalization. Her cardiac function normalized with TTE performed prior to dismissal reporting EF of 55% and resolution of the prior regional wall motion abnormalities. Acute pancreatitis is an inflammatory process of the pancreas that is a response to the inappropriate activation of proteolytic enzymes. Approximately 15–20% of cases can be classified as severe pancreatitis and these cases can be complicated by systemic inflammatory response syndrome (SIRS), sepsis, multiple organ dysfunction, and death; with mortality rates of 10–30%. This is the first report of severe pancreatitis complicated by "broken heart syndrome". One postulated mechanism for this disorder is catecholamine induced microvascular dysfunction resulting in myocardial stunning. It is hypothesized that this case was a result of sympathetic hyperactivity secondary to the inflammatory response from severe pancreatitis.

## 435

### An Uncommon Cause of Lower Gastrointestinal Bleeding

*Gautam Dutta, MD\*, Mukta Panda, MD, FACP. Internal Medicine, University of Tennessee College of Medicine, Chattanooga Unit, Chattanooga, TN.*

**Purpose:** Discuss the common causes and investigational modalities for lower gastrointestinal (LGI) bleeding.

Discuss the common presentation of LGI carcinoid tumors.

**Case:** A 44 year old male, recent immigrant from India, presented with copious melena for 1 day without abdominal pain, hematemesis, fever, weight loss, change in bowel habits. On presentation he was tachycardic (pulse 115/min), and hypotensive (BP 80/55 mmHg). Complete physical examination was unremarkable. Rectal exam showed frank blood. His Hb was 8.1 gm/dl and Hct was 25.1%. Panendoscopy revealed an ileal bleeding mass. Interestingly a colonoscopy done 6 months earlier in India for anemia workup was normal. Emergent laparotomy revealed numerous smaller intraluminal nodules scattered throughout the small bowel. Histopathology revealed carcinoid tumor. CT suggested possible metastasis to lymph nodes without liver involvement. He denied symptoms of carcinoid syndrome and his 24 hr urine 5-HIAA level was 13.1 (diagnostic > 25 mg/24 hr).

**Discussion:** The etiology of massive LGI bleeding includes diverticulosis, angiodysplasia, polyps, dieulafoy's lesion, infectious or inflammatory bowel disease. Small intestinal carcinoid tumors usually present around sixth decade of life with abdominal pain or obstruction and rarely with LGI bleeding. Less than 10% patients develop carcinoid syndrome. Our patient was unique as he was younger, without typical symptoms – rather presented with massive LGI bleed. Because of substantial false-negatives on initial endoscopy as demonstrated in our patient, the fact that small bowel carcinoid tumors are highly infiltrating; early diagnosis is mandated. An aggressive approach should be taken which would include repeating routine endoscopies, enteroscopy, capsule endoscopy, mesenteric angiography, and radionuclide RBC scan.

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**Band of Cacophony**

Gautam Dutta, MD\*, Aparna S. Chowdhury, MD, Mukta Panda, MD, FACP. Internal Medicine, University of Tennessee, Chattanooga, TN.

**Purpose:** Discuss the complications of Meckel's Diverticulum (MD), a rare occurrence in the adult population.

**Case:** A 55 year old white male presented with progressively worsening abdominal pain for 3 days. The pain started in the mid-lower abdomen and then became generalized, sharp and colicky, 10/10 in intensity, non-radiating, associated with nausea but no vomiting. Though he has noticed blood in his stools occasionally in the past, his last bowel movement was three days prior with semisolid stool without any blood. His past medical history is significant for hypertension and peripheral vascular disease, status post aorto-femoral bypass graft 6 yrs prior. On presentation his vitals were within normal limits, abdomen was non-distended but tender and rigid all over, more on left lower quadrant without any rebound tenderness. Bowel sounds were hypoactive. Rectal exam showed an empty vault. WBC count was  $9.0 \times 10^3/\text{mm}^3$  with 94.5% neutrophils, Hb of 9.0 gm/dl and Hct of 31.3%, liver and pancreatic enzymes were not elevated. ABG didn't show any acidosis and lactic acid level was not elevated. X-ray showed a non-obstructive bowel pattern without any free air. Abdominal CT showed findings consistent with complete mid to distal small bowel obstruction secondary to a closed loop obstruction. Emergent laparotomy showed a MD that had formed a band around a portion of small bowel causing it to twist upon itself and become necrotic. Histopathology showed MD with hemorrhagic necrosis and benign intestinal tissue with necrosis.

**Discussion:** Based on autopsy studies and intra-operative evidence, MD occurs in 0.3% to 4% of the population and is the most prevalent congenital anomaly of the gastro-intestinal tract. The lifetime risk of complications of MD is 4% which include obstruction, intussusception, inflammation, perforation, hemorrhage and neoplasm. Most patients who develop symptoms are younger than 10 years. So traditionally it is considered a disease of the pediatric age group and a less common consideration in the adult and geriatric population. Misdiagnosis occurs frequently in this age group because of the poor sensitivity of diagnostic tests, nonspecificity of complaints, and lack of recognition that this anomaly can present in the older age group. Physicians need to be cognizant of the multivariate ways of presentation of this commonly assumed pediatric disease especially when evaluating older age group patients for unexplained acute or intermittent abdominal pain, nausea and vomiting, rectal bleeding, peritonitis, or obstruction.

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**Gastroduodenal Crohn's Disease (GD CD): A Case of Dramatic Response to Selective Granulocyte-Monocyte Apheresis (GMA)**

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**Purpose:** GD CD, a rare and difficult to treat manifestation of Crohn's disease. We report the first case of a dramatic clinical, endoscopic and biochemical response of GD CD to selective GMA (Adacolumn).

**Case Report:** A 37-year-old man presented with cramping abdominal pain, diarrhea, occasional nausea and vomiting of 2 months' duration with a normocytic anemia (Hemoglobin 12 g/dl, MCV 85 fL) and guaiac positive brown stool. Colonoscopy revealed circumferential and longitudinal deep ulcerations with cobblestoning of ascending colon and a stenotic ileocecal valve. Biopsies showed chronic colitis without granulomas. An upper GI and small bowel (SB) series revealed irregular nodular thickening of the distal ileal loops, thumb-printing, narrowing and non-distensibility of proximal ascending colon consistent with Crohn's ileitis and colitis. Labwork revealed an elevated C-reactive protein (CRP) (97.5 mg/L; normal, 5 mg/L), erythrocyte sedimentation rate (ESR) (47 mm/hr; normal <15 mm/hr), pos-

itive ASCA IgG/IgA and a negative pANCA. Gastric and duodenal bulb ulcerations were found on gastroscopy with chronic inflammation without granulomas or *H. pylori*. Despite mesalamine, rifaximin and esomeprazole, at one-month follow-up, the patient's persistence of cramps and frequent bowel movements prompted an investigational study of 10 weeks of IRB approved Adacolumn with informed consent, while continuing his original medications. About 10 months after the original gastroscopy, a follow up gastroscopy showed remarkable disappearance of ulcerations from the stomach and the duodenal bulb. At this point, the patient had also received 5 weeks of low-dose 6-MP. Repeat ESR and CRP were normal.

**Discussion:** GD CD is a rare and difficult to treat form of Crohn's disease. Investigational technique of GMA involves the extracorporeal passage of peripheral blood through a column of cellulose diacetate beads (Adacolumn) or a nonwoven polyester fiber filter (Cellsorba) for "quantitative" removal of activated circulating leukocytes. We report a dramatic clinical, biochemical and endoscopic response to GMA, unlikely to be attributable to the 5-week course of low-dose 6-MP. GMA seems to be a promising "non-drug", sustained therapeutic approach for treatment of GD CD.

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**A Patient with Diarrhea and an Abnormal CT Enterography**

Rami J. Badreddine, MD, Conor G. Loftus, MD, Santhi S. Vege, MD\*. Gastroenterology and Hepatology, Mayo Clinic Rochester, Rochester, MN.

**Purpose:** A 35 years- old lady presented to the gastroenterology clinic with symptoms of early satiety, bloating, nausea, episodic abdominal pain and a 15 pound- weight loss of several months duration. She reported severe diarrhea. Workup included a 24 h alpha1- antitrypsin stool clearance which returned abnormally high.

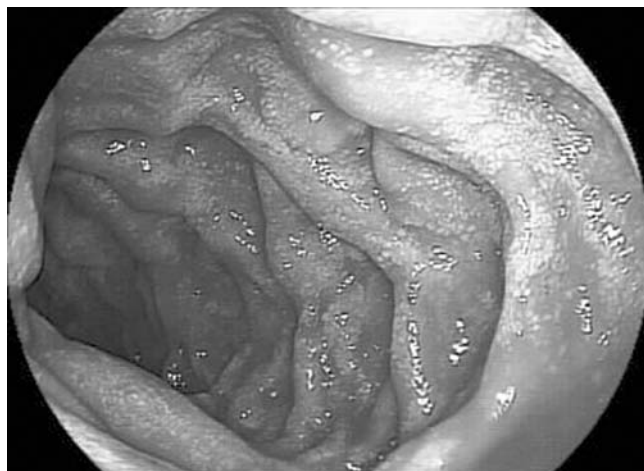
A CT enterography (Fig. 1) showed prominent gastric mucosal enhancement, mild enhancement in the duodenum and jejunum with thickening of the bowel wall suspicious for intestinal lymphangiectasia.

An upper endoscopy showed prominent diffusely scattered white spots in the first and second parts of the duodenum with a snowflake like appearance (Fig. 2). Biopsies from the second part of the duodenum were consistent with intestinal lymphangiectasia.

**Discussion:** Intestinal lymphangiectasia is characterized by ectasia of enteric lymphatic vessels in the mucosa and/or submucosa. When primary, it is usually associated with abnormal lymphatics elsewhere in the body. Secondary lymphangiectasia is usually caused by cardiac disease, inflammatory processes or toxic substances.

Very little information exists on the CT enterography appearances in this disease. The pattern described above on CT enterography, though not specific, should raise the suspicion for lymphangiectasia in the right clinical setting.





Clinical presentation ranges from diarrhea to significant weight loss, abdominal pain and chylous ascites. Diagnosis relies on clinical, laboratory, imaging and endoscopic findings. Classic endoscopic findings include diffusely scattered white spots representing dilated lacteals. Treatment relies mainly on dietary modification with a low fat, MCT and a high protein diet. TPN is sometimes required. Treatment of the primary cause is essential in secondary intestinal lymphangiectasia. The disease usually requires long term treatment although occasional remissions have been described.[figure1][figure2]

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#### Gastrointestinal Histoplasmosis

Navin Paul, MD, Subramanian Swaminathan, MD, Alka Ganesh, MD, George Abdelsayed, MD\*. Bridgeport Hospital [Yale New Haven Health], Bridgeport, CT and Christian Medical College, Vellore, India.

**Purpose:** A 43 y/o man from Bangladesh came with 4 month fever, low appetite and 9 kg weight loss. Investigations in his home country were noncontributory. He had received antimalarial and antituberculous drugs with no improvement. Initial examination showed low grade fever, tachycardia, emaciation, and hepatosplenomegaly. Investigations were normal except for AST 58 U/L, ALT 50 U/L, albumin 2.9 g/L, alkaline phosphatase[ALP] 312 U/L, and GGT 88 U/L. HIV ELISA, ANA, and infective workup were negative. USG abdomen showed hypoechoic splenic lesions, bilateral adrenal enlargement with calcification, and enlarged paraaortic nodes. US guided biopsy of paraaortic nodes revealed *Histoplasma capsulatum*. Itraconazole was started and patient became afebrile. While discharge was being planned,

he developed melena. EGD revealed a sinus in the duodenum [Fig. 1], which was seen to communicate with the right adrenal gland on CT abdomen. Biopsy of sinus wall showed *H. capsulatum*. Since he was also noticed to be icteric, LFT was repeated: total and direct bilirubin 5.5 and 4.7 mg/dL; AST 67 U/L; ALT 38 U/L; and ALP 743 U/L. ERCP showed hemobilia with blood clots obstructing the ampulla [Fig. 2]. Clots were removed and CBD was stented. Subsequent mesenteric angiography showed pseudoaneurysm of right hepatic artery which was coil-embolised. He was discharged on itraconazole. At 6 month follow up, his splenic and adrenal lesions had resolved. Northeast India and Bangladesh are emerging hotspots for histoplasmosis. GI tract [usually terminal ileum and colon] is involved in over 50% with disseminated histoplasmosis. Duodenal involvement is rare. Also fistula formation usually involves thoracic structures. This case represents the first report of fistulising GI histoplasmosis in an immunocompetent patient, and also the first report of a mycotic aneurysm in histoplasmosis.[figure1][figure2]



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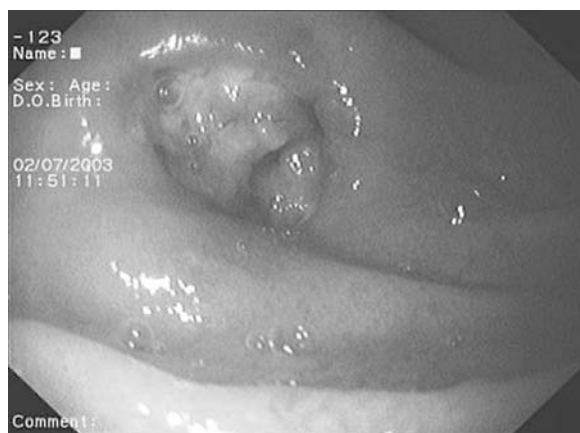
#### A Rare Cause of Rectal Bleeding!

Mitesh B. Patel, MD, Shilpa R. Gowdanapulya, MD, Rosena Custodio, MD, Jyothi A. Reddy, MD, FACG\*. Gastroenterology and Pathology, University of Illinois College of Medicine Urbana Champaign, Danville, IL.

**Purpose:** The presence of **gastric mucosa in the rectum is an extremely rare** clinical entity with only **29 cases** reported in the English literature. Heterotopia refers to the displacement of an organ or part of an organ from its normal site. Heterotopia is the result of primary displacement or a developmental abnormality where the foreign tissue is termed "heterotopia." Gastric heterotopia in the rectum can clinically present with hematochezia, but other complications such as rectovesical and anocutaneous fistula have been reported. We report a rare case of gastric heterotopia of rectum accompanied by a brief review of the available literature.

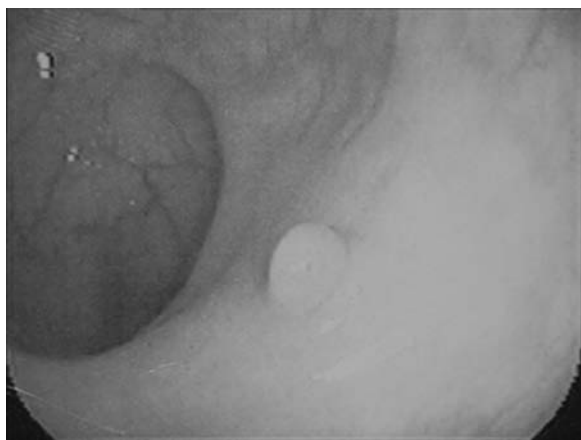
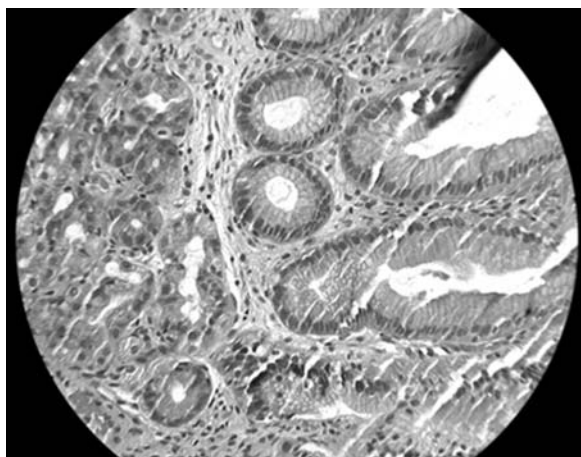
**Methods:** Chart review and review of literature using Medline and relevant bibliographies.

**Results:** A 49 year old man was referred to the gastroenterology clinic with complaints of rectal bleeding since three months. Approximately 18 months ago, the patient had a normal colonoscopic exam which was performed as a work up for abnormal bowel habits. Upon presentation, a repeat colonoscopy revealed a 3 mm sessile polyp in the distal rectum. No other anorectal pathology was evident to explain the symptoms of hematochezia.



The rectal polyp was resected using electrocautery snare. The pathology report of the polyp showed fragments of gastric mucosa suggestive of heterotopia.

**Conclusion:** The common presentations of gastric heterotopia of rectum are rectal bleeding and tenesmus, but patients may present with abdominal pain or incidental mass on colonoscopy. Hematochezia usually responds to treatment with histamine 2 receptor blockers, but endoscopic or surgical excision is the treatment of choice. The literature suggests that even an incidentally discovered gastric heterotopia of rectum in an asymptomatic patient should be removed in view of possible complications such as malignant degeneration and fistula formation.[figure1][figure2]



Administration of intravenous metronidazole 500 mg and ceftazidime 2 g every 8 hours was added. However, abdominal pain and distention worsened. A computed tomography (CT) scan revealed colonic wall thickening consistent with pancolitis, and an exploratory laparotomy revealed a grossly edematous colon, prompting a loop ileostomy. Postoperatively, intravenous metronidazole and ceftazidime were continued, and vancomycin 500 mg was administered t.i.d. by retention enema. Abdominal pain and distention stabilized but did not resolve. A follow-up CT scan revealed persistent colonic wall thickening, and a sigmoidoscopy revealed persistent pseudomembranous colitis 10 days postoperatively. In addition, the colonic fluid remained positive for *C. difficile* toxin A. Rifaximin 400 mg was added to vancomycin 500 mg and coadministered t.i.d. as a retention enema. Abdominal pain resolved and distention improved after administration of 4 rifaximin plus vancomycin combination enemas, and colonic fluid was negative for *C. difficile* toxin after 8 enemas. In addition, colonic wall thickening and ileus completely resolved. The patient was discharged 7 days after beginning combination enema therapy, with instructions to continue administration of vancomycin enemas on a tapering-off schedule. Eight weeks after ileostomy, colonoscopy was normal, and uneventful takedown of the ileostomy was performed 1 week later. Currently, the patient has normal bowel function and remains asymptomatic. This case represents the first documented use of a rifaximin enema and suggests that rifaximin 1200 mg/d is a successful treatment option for immunocompromised patients with CDAD refractory to conventional antibiotic therapy. Large, controlled clinical studies are warranted to confirm the beneficial role of rifaximin in CDAD.

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##### **Rectal Bleeding: A Case Report of Localized AL Amyloidosis of the Colon**

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**Purpose:** Primary (AL) amyloidosis is usually classified as a systemic disease involving multiple organ systems. Patients present with weakness, fatigue, and weight loss. Treatment for primary systemic amyloidosis includes hematopoietic cell transplant, clinical trials, or melphalan/dexamethasone and the prognosis is poor. AL amyloidosis can also be a localized disease. We present a case of localized AL amyloidosis of the colon.

**Case Report:** A 57 year old male complained of rectal bleeding for the past 3 weeks. He noted frank blood on the toilet paper as well as mixed in his stool. He otherwise was feeling well and denied joint pain, iritis, and any skin lesions. He had a similar episode 5 years prior. At that time, he underwent a colonoscopy with biopsies which were non-diagnostic. He was started on mesalamine but only took the medication for 3 weeks time as his rectal bleeding resolved. He reported no family history of inflammatory bowel disease. Laboratory studies including a CBC and CMP were within normal limits. His colonoscopy revealed patchy non-specific lesions involving the distal 50 cm of his colon. Biopsies were obtained and showed amorphous globular material in the lamina propria, vessel walls, and muscularis mucosae. It stained positive for amyloid. Further immunohistochemical stains were positive for primary or AL amyloidosis of lambda light change type. The patient was referred to Hematology for further work-up of amyloidosis. He underwent extensive testing which was negative for systemic amyloidosis, thus leaving the patient with a diagnosis of localized AL amyloidosis of the colon.

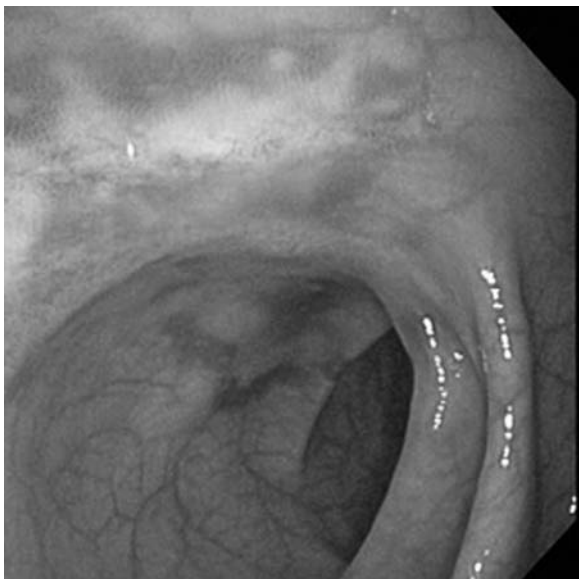
**Discussion:** Localized AL amyloidosis of the colon is an uncommon disease. Unlike systemic amyloidosis, it has an excellent prognosis. Since both localized and systemic AL amyloidosis can affect the colon, it is important to distinguish between the two for prognostic and treatment implications. Patients found to have only localized disease of the colon may require localized treatment such as argon plasma coagulation to control bleeding but they do not require systemic treatment. Due to the lack of long-term data, it is unknown if these patients should undergo periodic surveillance for systemic amyloidosis.[figure1]

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##### **Addition of Rifaximin Enema Resolves Colitis Associated with *Clostridium difficile* Infection**

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**Purpose:** Rifaximin is a nonsystemic, gastrointestinal-specific antibiotic and a promising therapeutic agent for *C. difficile* infections. This is a case report of a 37-year-old female who developed *C. difficile*-associated diarrhea (CDAD) 32 days after she received an allogeneic stem cell transplant for acute lymphoblastic leukemia. She had been taking immunosuppressive therapy (prednisolone, sirolimus, and tacrolimus) and had no prior history of gastrointestinal disease. The diagnosis of CDAD was established by a positive result for *C. difficile* toxin A. The patient developed profound ileus 24 hours after beginning oral vancomycin 125 mg q.i.d. as treatment for CDAD.



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#### Microscopic Papillary Adenoma as a Cause of Recurrent Acute Pancreatitis

Ana Ignjatovic, BMBCh, Anthony S. Mee, MD\*. Gastroenterology, Royal Berkshire Hospital, Reading, United Kingdom.

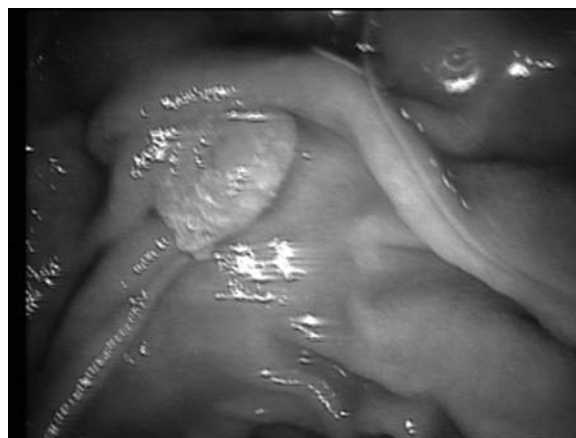
**Purpose:** 10–30% of patients with acute pancreatitis do not have demonstrable aetiology and are classified as having idiopathic acute (recurrent) pancreatitis (IAP or IARP). They should undergo full endoscopic evaluation in an attempt to delineate the aetiology. We present a case of IARP secondary to a microscopic adenoma but with normal cross-sectional imaging and macroscopically normal ERCP.

A 52-year-old man presented with his third episode of acute pancreatitis in a year. Repeated abdominal USS, CT and MTI scans of the pancreas revealed changes of acute pancreatitis but no gall stones or structural anomalies of the pancreas or the biliary tree. There were no risk factors for recurrent pancreatitis. He went on to have an ERCP. The procedure revealed a macroscopically normal duodenal papilla (see Fig. 1) with undilated biliary tree and a normal pancreatic duct (Fig. 2). Biopsies were taken from the duo-

denal papilla. Histology revealed cytoarchitectural changes compatible with an adenoma. The patient went on to have a surgical ampullectomy.

A handful of cases of recurrent acute pancreatitis secondary to a benign neoplasm of ampulla of Vater have been reported. We present a case of IARP with a macroscopically normal papilla and biliary tree. The diagnosis and histology are usually provided by the ERCP, but in a series of 52 patients in France who were found to have biopsy proven ampullary adenomas or carcinomas, 37% had endoscopically normal looking papilla. It is well acknowledged that the patients found to have dilated biliary tree and a macroscopically normal papilla should have sphincterotomy and intraampullary biopsies and if papillary adenomas detected it should be resected.

We propose that all patients who undergo ERCP for IARP and in whom no cause has been found have ampullary biopsies even if the biliary tree, pancreatic duct and ampulla appear macroscopically normal.[figure1][figure2]



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#### Hemobilia Post Intrabiliary Photodynamic Therapy (PDT) for Cholangiocarcinoma

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**Purpose: Case 1:** A 61 years old lady presented with jaundice and was diagnosed with an unresectable Klatskin tumor. She underwent CBD stenting and 2 cycles of intraductal PDT. She presented 6 weeks after her second cycle with severe hematemesis. An EGD revealed hemobilia (Fig. 1). Angiography showed pseudoaneurysms from both the right hepatic artery and the accessory right hepatic artery (Fig. 2). These were embolized and the patient's bleeding stopped.

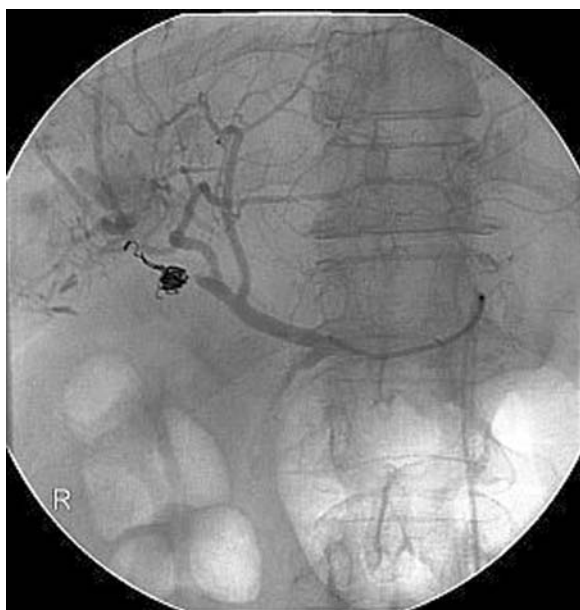
**Case 2:** A 53 years old male with ulcerative colitis and PSC was found to have a hilar, non resectable cholangiocarcinoma. He underwent a transcutaneous cholangiogram and biliary drain placement. An abdominal MRI done for staging showed a large left hepatic artery pseudoaneurysm which was successfully embolized. Two weeks later he underwent transcutaneous PDT. He presented 48 hours later with massive hemobilia through his drain. Angiography revealed bleeding from an aneurysm around the previous embolization site of the left hepatic artery as well as from new collaterals from the right hepatic artery. This was successfully injected with Ivalon particles.

**Discussion:** We presented two cases of hemobilia from hepatic artery pseudoaneurysms following intrabiliary PDT. When reviewing the literature for reported complications of intrabiliary PDT we found very few cases of hemobilia.

It is unclear if bleeding is the result of the radiation from PDT itself or whether other mechanisms are involved. We think that patients with known or suspected hepatic artery pseudoaneurysms or aneurysms should undergo



treatment for these by an expert interventional radiologist before proceeding with PDT. We cannot recommend routine angiography prior to PDT in all patients at this time.[figure1][figure2]



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### Carcinosarcoma: An Unusual Hepatic Metastasis

Anastasia C. Waechter, MD\*. *Gastroenterology and Hepatology, Stanford University Medical Center, Stanford, CA.*

**Purpose:** Carcinosarcomas are rare tumors with malignant epithelial and mesenchymal components, which most commonly originate in the uterus and ovary. I describe a case of carcinosarcoma of presumed gynecologic primary presenting as a symptomatic hepatic metastasis and review the approach to focal liver lesions.

**Methods:** A 76-year-old woman presented with right-sided pleuritic subcostal pain. A CT angiogram-thorax revealed a 2.7 cm × 2.7 cm hypodense lesion in the hepatic dome. On biphasic CT-abdomen, this appeared to be an atypical hemangioma. The patient had no known or suspected extrahepatic malignancy. Laboratory evaluation for underlying liver disease and AFP

were normal. A 3-month follow-up CT revealed increased size and new peripheral areas of enhancement, concerning for malignancy.

One week later, the patient developed recurrent pain. Repeat CT showed acute hemorrhage into the lesion. She underwent urgent surgical resection of a hemorrhagic mass from the hepatic dome. Histology revealed high-grade CK7+/CK20- glands in a high-grade PASD+ spindle cell background consistent with carcinosarcoma, most likely of ovarian or endometrial origin. Serum CA-125 level was elevated at 336 (normal <35 U/ml). A postoperative CT chest/abdomen/pelvis and CT-PET scan revealed pathologic right iliac and inguinal lymph nodes. An FNA of the inguinal lymph node revealed high-grade carcinoma. No primary tumor was found on CT scan or endovaginal ultrasound. However, this was considered most likely a metastatic carcinosarcoma of gynecologic origin.

The patient received gemcitabine and carboplatin with initial response. She is currently asymptomatic, but her most recent imaging shows increasing pelvic lymphadenopathy. She is being evaluated for radiotherapy.

**Conclusion:** Focal hepatic lesions may be found on imaging exams done to evaluate symptoms but more often are found incidentally. The differential diagnosis is broad and includes benign causes (cysts, hemangiomas, adenomas, FNH, and abscesses) as well as malignant causes, with metastases being the most common hepatic malignancies. The correct diagnosis of solitary liver lesions depends upon the clinical context in which the lesion was detected. Important factors include patient age, gender, symptoms, history or risk factors for chronic liver disease and history or suspicion of extrahepatic malignancy. Radiographic features in combination with clinical history and serum tumor markers can establish the diagnosis in the majority of patients without the need for fine needle biopsy.

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### Human Small Intestinal Anisakiasis Due to Consumption of Raw Sardines

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**Purpose:** Anisakiasis is a human parasitic disease caused by the ingestion of raw fish. The diagnosis of gastric anisakiasis can be easily confirmed by endoscopy. However, small intestinal anisakiasis is difficult to diagnose because of the absence of appropriate diagnostic modalities. We describe two cases of small intestinal anisakiasis, emphasizing the usefulness of MDCT (Multidetector-row CT) in the diagnosis.

**Case1:** A 64-year-old Japanese man was admitted to our hospital because of sudden abdominal pain and vomiting. Two days prior to admission, he had eaten raw sardines as *sashimi*. Abdominal roentgenogram showed air-fluid levels, suggesting intestinal obstruction. MDCT clearly demonstrated segmental, symmetrical, and circumferential wall thickening and a small amount of ascites. Fluid replacement and resting immediately relieved his symptoms. The anti-anisakis antibody titers in paired sera were measured.

**Case 2:** A 70-year-old Japanese man was admitted to our hospital because of sudden abdominal pain and vomiting. Two days prior to admission, he had eaten raw sardines as *sashimi*. Abdominal roentgenogram showed air-fluid levels, suggesting intestinal obstruction. Because of his past history of appendectomy, a diagnosis of small intestinal obstruction due to adhesion might have been reasonable. However, considering his recent history of ingesting of raw sardines and MDCT findings, a diagnosis of human intestinal anisakiasis was indicated. Fluid replacement and resting immediately relieved his symptoms. The anti-anisakis antibody titers in paired sera were measured.



**Discussion:** In Japan, there is a long-standing tradition of consuming raw fish, and gastric anisakiasis accounts for 95.6% of cases, intestinal anisakiasis for 4.1%, and that at other sites for 0.3%, according to the analysis of a series of 15,715 cases. As raw fish dishes are gaining popularity in many countries, the frequency of anisakiasis is likely to increase. Anisakiasis should be considered in the differential diagnosis of small intestinal obstruction.

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#### Cholestatic Jaundice as a Paraneoplastic Presentation of Hodgkin's Lymphoma

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**Purpose:** A 21 year old female was transferred to our hospital for the management of hyperbilirubinemia in the setting of a recent diagnosis of Hodgkin's disease. Upon initial assessment, laboratory workup revealed cholestasis with elevated transaminases, alkaline phosphatase, and no coagulopathy. The rest of the workup was negative. Abdominal imaging was negative. Her bilirubin continued to rise, and a liver biopsy showed pericentral cholestasis and mild non-specific lobular inflammation. She was started on prednisone with a gradual taper. Six weeks into treatment, her jaundice resolved.

Hodgkin's disease-related cholestasis has multiple pathophysiologic mechanisms. The differential diagnosis of jaundice in a lymphoma patient includes the more common etiologies of sepsis, drugs, viral infections and hepatic metastasis. These diagnoses can usually be ruled out with an extensive initial workup. However, liver involvement in Hodgkin's disease (HD) can be a more subtle finding that requires a prompt and a more invasive workup. The three main causes of intrahepatic cholestasis in association with lymphomas are hepatic lymphoma, vanishing bile duct syndrome (VBDS) and a paraneoplastic phenomenon. Secondary hepatic lymphoma is almost always an end-stage manifestation of the disease that can rapidly progress into fulminant hepatic failure. Primary hepatic lymphoma, on the other hand, occurs in the absence of extrahepatic disease. It has an extremely dismal prognosis. VBDS is another cause of cholestasis that has been associated with HD. Histologically, this entity is characterized by the absence of bile ducts in the portal triads. Treatment with steroids, ursodeoxycholic acid and IVIG has been described with not enough evidence to advocate the use of either therapy. The last mechanism is due to a paraneoplastic effect. Stauffer described a syndrome of nonmetastatic nephrogenic hepatic dysfunction in association with renal cell carcinoma. Later on a similar paraneoplastic cholestatic entity has been described in association with multiple malignancies including lymphoma. The proposed mechanism for this rare entity could be overexpression of IL-6 by the tumor cells, and hence the reported literature on the improvement of the cholestasis after treating the malignancy.

**Conclusion:** In conclusion, the possibility of hepatic lymphoma, VBDS or a paraneoplastic mechanism should be considered in every case of jaundice and HD. This can be a life threatening complication that can progress to fulminant hepatic failure short of early and appropriate intervention.

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#### Rare Case of Lung Cancer Metastatic to the Colon Incidentally Discovered at Screening Colonoscopy

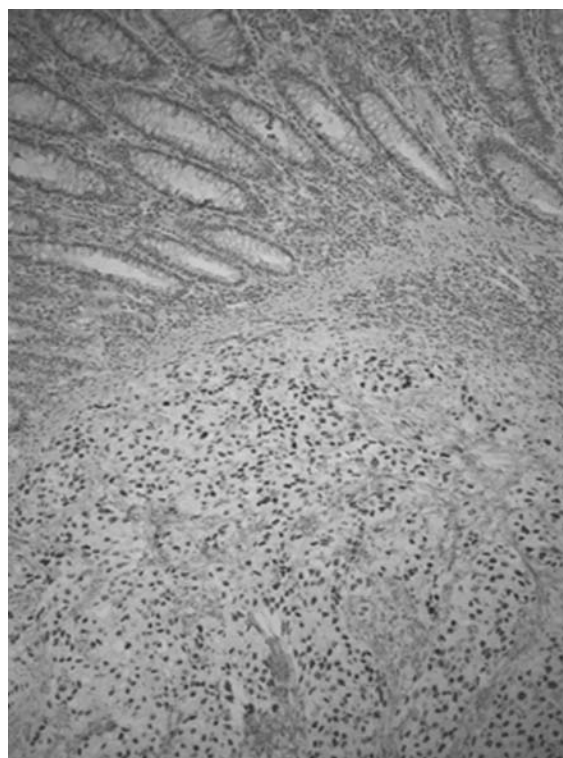
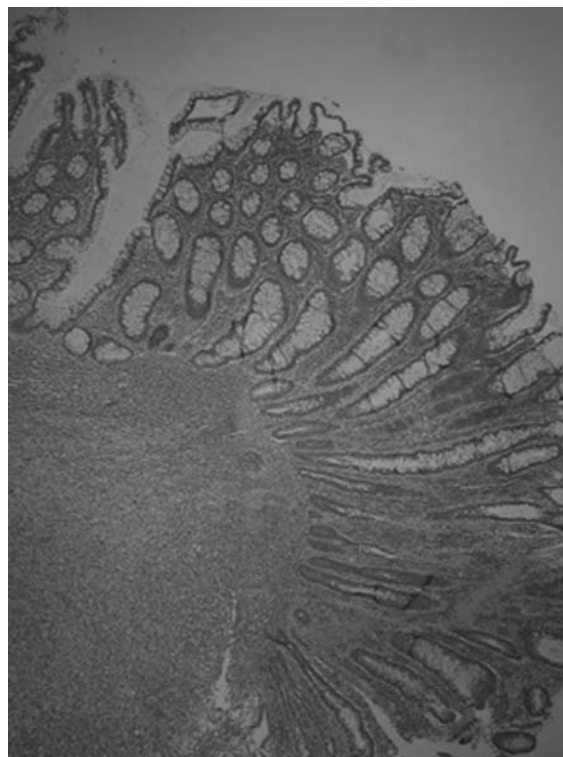
Gennadiy Bakis, MD, Matthew M. Baichi, MD\*. *Gastroenterology, Division of Gastroenterology, Hepatology, and Nutrition, Buffalo, NY.*

**Purpose:** The gastrointestinal tract is a rare site for lung cancer metastasis. Involvement of the colon is especially rare and is usually symptomatic and discovered after detection of the primary tumor. We report a case of lung cancer metastatic to the colon discovered at screening colonoscopy.

**Methods:** Case report

**Results:** A 71 year old male presented for colonoscopy based on Guaiac positive stool testing performed as part of routine colon cancer screening. Laboratory evaluation showed no anemia.

Colonoscopy revealed a transverse colon mass. Biopsy showed colonic mucosa with no evidence of dysplasia. Tumor stains suggested undifferentiated





carcinoma, likely metastatic. CT scan of chest, abdomen and pelvis showed a right upper lung lobe soft tissue density. PET scan showed uptake in the right upper lung as well as right paratracheal and left neck areas. Resection was performed and pathology revealed the tumor to be submucosal in location (Fig. 1) with ulceration of overlying mucosa and extension into the subserosa. Immunohistochemical studies performed on representative tumor sections reveal a pattern suggestive of lung origin (Fig. 2). One out of seven lymph nodes showed metastatic carcinoma.

The patient underwent a CT-guided FNA biopsy of the right upper lung nodule. Immunohistochemical stains and morphologic features were similar to the colonic tumor; both were consistent with a lung primary.

The patient enrolled in a clinical trial and received Paclitaxel and Carboplatin chemotherapy. Interval chest CT scan 3 months after initiation of chemotherapy showed decrease in the size of the lung mass, but treatment was stopped because of neuropathy. The patient expired 8 months after presentation.

**Conclusion:** To the best of our knowledge this is the first report of lung carcinoma with colon metastasis discovered at screening (FOBT positive) colonoscopy.[figure1][figure2]

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### Acute Noncholestatic Azathioprine Induced Hepatotoxicity in a Female with Crohns Disease

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**Purpose:** The patient is a 34 yo female with ileocolonic Crohns Disease (CD) since age of 19. She had undergone terminal ileum resection & subtotal colectomy with ileostomy & Hartmanns pouch reconstruction 10 years ago. With complaints of watery rectal drainage, colonoscopy was performed & suggested acute on chronic inflammatory changes of the pouch. She was started on Azathioprine (AZA) 100 mg/day. Two weeks later she presented with 2 days of abdominal pain, nausea, & non-bilious emesis. She denied use of alcohol, IV drugs, acetaminophen, or herbals. No sick contacts, fever, or recent traveling. On presentation she was hypotensive and tachycardic. No signs of encephalopathy or jaundice. Abdominal exam revealed shock-fist tenderness & normal liver span. Rectal exam was unremarkable. Skin examination of extremities revealed tender erythematous nodules. Lab data revealed transaminitis without cholestasis. Toxicology screen, serologies for ANA, ASMA, AMA, EBV, viral hepatitis panel were negative. Iron & copper studies were unremarkable. She was homozygous for wild-type thiopurine methyltransferase. 6-thioguanine nucleotide was 99 (RI: 230–400) & 6-methylmercaptopurine was 1003 (RI: <5700). CT showed diffuse hepatic steatosis without focal lesions & patent portal and hepatic veins were seen on Doppler U/S. Skin biopsy showed Erythema Nodosum. Three days after discontinuing AZA & with supportive care, improvement was noted in liver biochemistries. This case of AZA-induced hepatotoxicity was unique in that liver toxicity reflected an abrupt non-cholestatic hypersensitive mechanism of hepatitis. Furthermore, low levels of 6-TGN & 6-MMP suggested low risk for toxicity, raising a suspicion for an unknown metabolic pathway by which AZA induces acute liver injury without cholestasis.[figure1]



### Laboratory Data During Hospital Stay

Day	1	2	3	4
AST	5978	2527	426	114
ALT	4858	3230	1893	1194
Alk. Phos	121	90	83	105
Bilirubin	1.6	1.40	0.9	0.6
Dir Bilirubin	1.2	1.1	N/A	0.4
Albumin	3.3	2.9	2.7	2.7
Creatinine	2.5	1.7	0.7	0.6
BUN	37	28	15	14
WBC	2.5	6.3	8.6	10.1
Hematocrit	44.8	35.1	32.5	30.9
Platelet	231	197	210	180
PT	25.2	28.9	19.1	16.8

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### The Use of a Self-Expanding Plastic Stent for an Iatrogenic Esophageal Perforation

John M. Petersen, DO\*. Gastroenterology, Baptist Medical Center/Borland-Groover Clinic, Jacksonville, FL.

**Purpose:** A 48 year old woman was diagnosed with an ascending colon carcinoma six months earlier. The disease had metastasized to the axial and peripheral skeleton in numerous locations. Radiation therapy was administered to the cervical and thoracic spine with 30 fractions of 180G each. Within six weeks of completion, the patient developed dysphagia, chest discomfort, bouts of regurgitation, nausea, and lost 15 pounds. An EGD revealed a tight, inflammatory, likely radiation-induced stricture in the distal esophagus that had narrowed the lumen to 8 mm. A CRE balloon dilation was carried out under direct vision to 13 mm. She developed chest pain in the recovery area, and a Hypaque esophagogram confirmed a perforation. A naso-gastric tube was placed endoscopically, and she received broad spectrum antibiotics and IV hydration. Within 24 hours, a Polyflex stent, 18 mm in the body, 23 mm at the proximal opening, 9 cm long (Boston Sci., Natick, MA) was placed, and attached to the proximal esophagus with nylon ligatures and Resolution hemostatic clips. The patient was able to eat soft solids within 48 hours, and was discharged on the fourth day. She gained weight and had no chest pain or dysphagia. Chemotherapy was initiated due to an abnormal PET/CT, and a rising CEA. The stent was removed 7 weeks later, and endoscopically the perforation had sealed, with an inflammatory mucosa and an intact lumen left behind.

For years, self-expanding metal stents (SEMS) have been deployed in the esophagus for malignant obstruction, as well as to cover post-operative leaks and fistulae. The use of SEMS for benign strictures has been met with a variety of complications and great difficulty in removal. The placement of removable Polyflex plastic stents across malignant strictures has been well recorded, while utilization for iatrogenic perforations is rare. The Polyflex is a polyester woven stent with a silicone covering, which makes for easy deployment, and simple endoscopic removal. Plastic stents are effective in bridging malignant strictures, fistulae, post-operative leaks, perforation following atrial fibrillation ablation techniques, benign inflammatory peptic strictures, and as shown in this vignette, post-endoscopic dilation perforations. The plastic Polyflex rapidly eliminates contamination of the mediastinum after perforation, allows for oral hydration and nutrition, and is easily removable. To avoid migration, which can be as high as 30%, we suggest ligature fixation with hemostatic clips.

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### Collagenous Gastroenterocolitis in a Two Year Old Boy with Cerebellar Ataxia

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**Purpose:** Collagenous colitis is usually diagnosed in adults, with normal appearance on endoscopy and rarely associated with small bowel inflammation. In pediatrics there are less than 10 reported cases. We report a case of collagenous gastroenterocolitis (C-GEC) in a 2-yr-old boy with cerebellar ataxia. He had a 2-mo history of watery stools and weight loss, 1 mo of emesis and fevers. Loperamide, and restriction of lactose and refined sugar did not alter the diarrhea. Initial studies showed low sodium and albumin, anemia, and elevated ESR. Despite bowel rest he had profuse diarrhea with a low fecal osmotic gap. All other stool studies were negative. He also had negative anti-enterocyte Ab, celiac panel, ASCA IgA, ANCA IgG, ANA and normal lymphocyte enumeration, total IgM and IgA, and complement levels. Abdominal CT showed dilated fluid filled bowel loops. Endoscopy revealed erythema and petechiae in the gastric body and increased vascularity, mild edema and erythema in the colon. Biopsies showed thickening of the subepithelial basement membrane (BM) ( $>5\ \mu$ ) in the stomach, duodenum and colon. There was also sloughing of the epithelium, abundant neutrophils in the lamina propria infiltrating the adjacent crypt and surface epithelium and reactive cellular atypia. Trichrome and immunohistochemistry for collagen 3 confirmed collagenous subepithelial thickening. Congo red staining for amyloid was negative. The diagnosis of C-GEC was made based on histologic appearance and stains. He was treated with 2 wks of IV steroids and bowel rest with symptom resolution. Repeat biopsies at the end of 2 wks revealed less inflammation but persistent presence of thickened BM throughout. The patient was treated with a PPI, mesalamine and 8 wks of oral steroids. During this period he tolerated a diet low in lactose and refined sugar and had resolution of anemia and hypoalbuminemia. 2 wks after finishing oral steroids, stools increased to 6 times a day. The patient then started on bismuth subsalicylate, which continued for four weeks with resolution of his symptoms. We were not able to associate his neurologic condition with the current problem. This case is unique as most adult cases have collagenous disease limited to the colon with less common reports of collagenous gastritis and even rarer reports of collagenous duodenitis. No other pediatric case has shown small bowel inflammation and duodenal collagenization.

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#### Refractory Rectal Ulcer Secondary to Infrared Coagulation Treated with Canasa Suppository

*Yaman Suleiman, MD, Samah Bassas, MD, Mohammad Alsolaiman, MD\*. Gastroenterology Dept, Central Utah Clinic, Provo, UT.*

**Purpose:** Rectal ulcer is an uncommon rectal disorder that can present with bleeding, passage of mucus, and sense of incomplete evacuation. Solitary rectal ulcer is the most common type of rectal ulcer. Other less common causes include infection, ischemia, idiopathic, radiation, malignancy or medications. Here we report two cases of rectal ulcers secondary to hemorrhoid treatment, treated successfully with Canasa suppository.

**Methods:** Two patients with grade II internal hemorrhoid treated with Infrared coagulation (IRC). Both patients developed rectal ulcer at the site of the application with intermittent bleeding. Initially they were treated conservatively with stool bulking agents and Anusol suppository, unsuccessfully. Canasa suppository were applied QHS for one month. Both achieved complete healing of there ulcers and symptoms.

**Results:** Both patients achieved complete healing of there ulcers and symptoms. Repeat flexible sigmoidoscopy showed complete healing of the ulcer. No further treatment was required.

**Conclusion:** Nonsurgical therapy for hemorrhoidal disease grades I and II with infrared photocoagulation, banding, bipolar and laser coagulation is a good alternative to surgery; it is painless, suitable as an outpatient procedure and its cost is low. These treatment are complicated occasionally with delayed rectal bleeding, urinary retention, pain, and fever. Treating this complication is very important for the practicing Gastroenterologist. Canasa is a new addition to our armamentarium for treating refractory rectal ulcers secondary to such hemorrhoidal treatment.

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#### Steroid Injection for Benign Refractory Pyloric Stenosis

*Yaman Suleiman, MD, Samah Bassas, MD, Mohammad Alsolaiman, MD\*. Gastroenterology Dept, Central Utah Clinic, Provo, UT.*

**Purpose:** Several studies have demonstrated good rates of success for the relief of symptoms from pyloric stenosis using through-the-scope balloons. Patients who require more than two dilations are at high risk of endoscopic failure and the need for surgical intervention. Here we describe two refractory patients treated endoscopically using steroid injection and therefore avoiding surgery.

**Methods:** Two patients presented with gastric outlet obstruction secondary to peptic ulcer disease. Both underwent multiple sessions of through the scope balloon dilation (average 4 sessions) with H. Pylori eradication and high dose PPI. Patients symptoms recurred with very short improvement after each dilation. First patient refused surgery, and the other one had severe comorbidities. 80 mg Kenlog injection was performed (20 mg in every quadrant of the pyloric opening) after performing balloon dilation. Both patients showed significant improvement with no need for further balloon dilation. Average follow up for these two patients was 18 months. Both patients were kept on PPI.

**Results:** Both patients showed significant improvement with no need for further balloon dilation. Average follow up for these two patients was 18 months. Both patients were kept on PPI.

**Conclusion:** Endoscopic balloon dilation has been used to treat patients with gastric outlet obstruction caused by peptic stricture. Surgery is associated with significant morbidity and mortality and should be reserved for endoscopic treatment failures. Benign pyloric stenosis can be readily treated with endoscopic balloon dilation and should be the first-line therapy. Steroid injection should be considered early in the paradigm of treating benign pyloric stenosis especially refractory cases and before consideration for surgery.

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#### Liver Abscess as a Complication of Esophageal Balloon Dilation

*Yaman Suleiman, MD, Samah Bassas, MD, Mohammad Alsolaiman, MD\*. Gastroenterology Dept, Central Utah Clinic, Provo, UT.*

**Purpose:** Despite the increase use of upper endoscopy, the complication rate has remained low. Infectious complications of EGD include transmission of infection by contaminated endoscopes or ancillary equipment, bacteremia and aspiration pneumonia. Here, we are reporting a liver abscess followed a routine upper endoscopy dilation in patient with gastric bypass.

**Methods:** A 59 year old patient with history of gastric bypass 19 years ago presented with intermittent dysphagia has been going on for the last few months. Her upper endoscopy was remarkable for schatzki ring and gastric pouch contained undigested food. The gastrointestinal anastomosis was patent. The schatzki ring was dilated using CRE balloon 15–18 mm with evidence of breaking the mucosa at 16.5 and 18 mm. Her other past medical history was significant otherwise for thyroid cancer, thyroidectomy 20 years ago, tobacco and ETOH abuse. Patient presented with right upper quadrant pain 2 days after the EGD to outside facility. She was treated symptomatically. Pain returned and patient developed fever and chills. CT scan of the abdomen performed at our facility 2 weeks after the EGD showed left hepatic lobe abscess. US guided drainage grew *Candida Albicans*, streptococcus Solivarius, and Beta Hemolytic Strep Group B. Esophagogram failed to show any leak or perforation. The abscess resolved with IV antibiotic and percutaneous drainage without the need for surgery.

**Results:** The timing between the onset of her symptoms and the EGD suggest causal relationship. This is most likely related to transient bacteremia secondary to the dilation. Her altered anatomy, gastroparesis and ETOH intake, probably predisposed her for the bacteremia and the immune suppression status.

**Conclusion:** Esophageal dilation has the highest incidence of bacteremia of all gastrointestinal endoscopic procedures, occurring in approximately 45 percent of cases. In spite of this, complications of bacteremia such as

endocarditis are rare. The most common reported complication is endocarditis, and less frequently meningitis. Antibiotic prophylaxis is not warranted in most patients undergoing esophageal dilation except for those at high risk. People with immunosuppressed status or altered anatomy might need to be considered for prophylaxis.

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### EUS in the Diagnosis of Pancreatic Duct Stone Presenting as Pancreas Divisum and Pancreatic Stricture

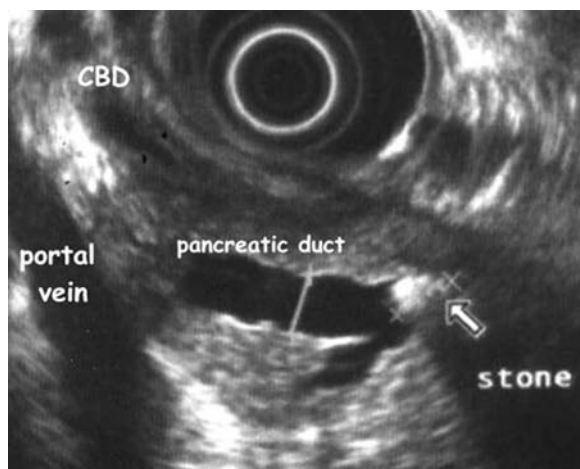
Kenneth Belitsis, MD\*, Rajiv Uppal, MD, Steven Gorcey, MD, Dawn Loveland, ANP. Monmouth Gastroenterology, Eatontown, NJ and Monmouth Medical Center, Long Branch, NJ.

**Purpose:** Evaluation of the peri-ampullary common bile duct (CBD) and pancreatic duct (PD) is notoriously insensitive using standard imaging techniques such as transabdominal ultrasound, CT, and MRI/MRCP. EUS is being used increasingly to compensate for this deficit and as an excellent means of imaging this area.

**Methods:** We present a 49 year old female who had a remote history of alcohol abuse. She suffered from multiple episodes of acute on chronic pancreatitis. An ERCP with brief pancreatic duct stenting performed a year prior provided temporary relief of her abdominal pain. Two MRCPs performed were interpreted as pancreatic duct dilation with pancreas divisum (*P. divisum*). A repeat ERCP attempt failed to successfully cannulate the PD due to suspected stricture with *P. divisum*. There was no mention of a stone or a mass on any of these studies. She presented to our institution with another episode of acute on chronic pancreatitis. Her serum lipase was 1186 u/L (normal: 9–50 u/L) and her amylase was 290 u/L (normal: 28–115 u/L). Liver function tests were normal.

**Results:** An EUS was performed. A single 8 mm stone was found obstructing the proximal PD at the peri-ampullary region. This dilated the PD to 8 mm including a branch within the head of the pancreas (Fig. 1). No strictures, no masses and no *P. divisum* were identified. We next performed an ERCP which revealed a single filling defect in the proximal PD consistent with the stone. A pancreatic sphincterotomy was performed and the stone was removed using a 1.5 cm Trapazoid™ Rx retrieval basket (Boston Scientific). The patient tolerated the procedure well and has been asymptomatic since.

**Conclusion:** This case demonstrates the superiority of EUS when evaluating the peri-ampullary area. The MRCPs erroneously interpreted the dilated PD in the head of the pancreas as *P. divisum* while the ERCPs erroneously interpreted the stone itself as a stricture. Both modalities failed to make the correct diagnosis. EUS should strongly be considered when evaluating diseases suspected of pancreaticobiliary origin and especially those affecting the peri-ampullary region.[figure1]



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### Superior Mesenteric Artery Syndrome

Angela M. Mills, MD, Dusan Stanojevic, Medical Student, Andrew D. Mills, MD, Syed T. Bin-Sagheer, MD\*. Internal Medicine, Division of Gastroenterology, Creighton University Medical Center, Omaha, NE.

**Purpose:** A 21-year old female with history of methamphetamine use presented with severe epigastric pain associated with nausea, vomiting, and rapid weight loss. Basic laboratory, HIV screening, and thyroid studies were unremarkable. The patient was admitted for symptom management and further diagnostic studies. Abdominal ultrasound unveiled massive gastric dilatation. CT scan revealed severe distention of the stomach and two thirds of the duodenum which was highly suspicious for SMA syndrome.

The SMA formed an angle of approximately 10 degrees (normal: 38–56 degrees) with the abdominal aorta, and the third part of the duodenum crossed caudal to the origin of the SMA, coursing between the SMA and aorta. Upper endoscopy demonstrated antral erosions but failed to reveal any mechanical causes of stomach and duodenal dilatation. Upper GI and small bowel series were consistent with SMA syndrome.

Non-bloody gastric fluid (2,500 cc) was removed on the first day of admission. Treatment was conservative and consisted of: nasogastric decompression, Hayes maneuvers, and fluids. Her symptoms markedly improved. After three days, the patient was started on an oral diet and discharged home.

**Discussion:** SMA syndrome was first described in 1861 by Von Rokitansky who proposed that duodenal obstruction was caused by arteriomesenteric compression. Precise incidence of this syndrome in the U.S. is unknown but some literature cites 0.013%. It is most common in women ages 10–30. Etiological factors include: anorexia nervosa, exaggerated lumbar lordosis, or depletion of mesenteric fat caused by rapid severe weight loss due to catabolic states such as cancer, surgery, burns, or psychiatric problems.

SMA syndrome is characterized by epigastric pain, nausea, voluminous vomiting of partially digested food, postprandial discomfort, and early satiety. The diagnosis requires utilization of CT scanning, upper GI series and upper GI endoscopy. Endoscopy confirms diagnosis and excludes other etiologies of duodenal compression.

Conservative treatment is initially recommended in all patients. This includes adequate nutrition, nasogastric decompression, and positioning of the patient in a left lateral decubitus position. In some patients, enteral feedings and parenteral nutrition is needed. Surgical treatment (duodenojejunostomy) is reserved for the patients not responsive to conservative management as well as for the patient with gradual onset of SMA syndrome.

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### Abdominal Wall Biloma Following Laparoscopic Cholecystectomy (LC)

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**Purpose:** Iatrogenic injury to the biliary tree is a well-documented complication of Laparoscopic CCY (LC). The widespread use of this surgery in the early 1990s led to increase in the frequency of biliary injury. With increasing experience, the incidence has declined to an overall incidence of 0.5%. Here we report an interesting case of biloma involving the abdominal wall following LC.

**Methods:** A 48 year old morbidly obese man underwent uneventful LC with normal cholangiogram for gallstone disease. His past medical history is significant for DM II and HTN. He was readmitted two days later for abdominal pain, abdominal distension and chills. On his exam, the abdominal wall was edematous with discolorization. Initially this was thought to be secondary hematoma. He was treated symptomatically with pain medication, IV antibiotics and bed rest. His abdominal pain and distension got worse and CT scan of the abdomen showed large fluid collection. US guided drainage proved the fluid to be of biliary nature. He underwent ERCP with stent placement because of the high clinical suspicion for bile leak. Occlusive cholangiogram failed to show free bile leak. Patient showed quick clinical

improvement and was discharged home two days after the ERCP, the stent was removed in 6 weeks without recurrence of his symptoms.

**Results:** Common causes of bile leak include cystic duct leak, common bile duct or hepatic duct injury or GB bed leak. In our case the fluid must have drained into the abdominal wall as proved by the CT scan. In contrast to open CCY, in which all abdominal wall layers are closed, the defects created by trocars in LC are left open. Also the CO<sub>2</sub> insufflated into the peritoneal cavity during LC can escape the peritoneal cavity and accumulate in the abdominal wall creating pseudo-pockets thus facilitating fluid collection. The proximity of the wound to the biliary ducts and/or GB bed may be contributing factors. Bile and bile duct leak should be considered in the differential diagnosis in addition to the hematoma in patients with abdominal wall edema after LC.

**Conclusion:** Successful management of bile duct injury requires a multidisciplinary team approach incorporating biliary endoscopists, interventional radiologists, and hepatobiliary surgeons. The approach to the patient depends upon the nature and extent of the injury, the presence or absence of biloma, and the timing of discovery.

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#### New Method for Esophageal Foreign Body Removal

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**Purpose:** Accidental foreign body or large food bolus ingestion occur mainly in children and in edentulous or mentally impaired elderly adults. Meat bolus impaction above a preexisting esophageal stricture or ring probably the most common cause of esophageal body obstruction in adults. Meat bolus disimpaction is one of the most challenging endoscopic procedure for the Gastroenterologist. Here we describe a new method.

**Methods:** An 83-year-old man presented with acute dysphagia symptoms for more than 24 hours duration after chicken meal. Prominent symptoms included inability to swallow, and cough. EGD revealed a total blockage of the lumen of the lower esophagus. Multiple attempts using Polypectomy Snare, Foreign body Forceps, and Roth Nets were unsuccessful to dislodge the meat bolus. Using Soehendra dilator a passage was created in the middle of the meat bolus. An 8–10 mm esophageal balloon dilator was passed distal to the FB through the created passage. After inflating the balloon, this was pulled proximally allowing the dislodge of the FB which passed spontaneously to the stomach. Our patient had a recent previous normal EGD which allowed us to exclude distal obstruction.

**Results:** Our patient did very well after the procedure. He underwent elective esophageal dilation later on of his esophageal peptic stricture. He was placed on long term PPI. He had no recurrent symptoms on one year follow up.

**Conclusion:** Because of the remarkable variety of articles and situations may be faced during foreign body removal, the endoscopist must be able to use various instruments to remove objects that lodge in the esophagus. The method described here has never been reported previously in the English literature. This method need to be applied carefully to avoid perforation. Applying this method under fluoroscopy could be useful, in difficult cases.

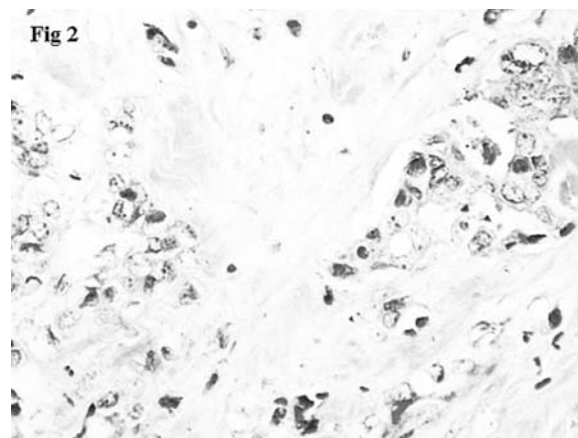
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#### A Rare Case of Intraluminal Ureter Metastasis from Rectal Cancer

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**Purpose:** Intraluminal metastasis to the ureter of rectal cancer is extremely rare. To the best of our knowledge, this is the third such case report. In 2003, a 49-year-old male was admitted to the hospital for eight-month history of dark bloody stools. CT scan revealed 3.1 cm circumferential mass

in the rectum with nodules of soft tissue with in the adjacent mesentery. There was no evidence of metastatic disease. Colonoscopy confirmed the circumferential mass in the rectum. Biopsy revealed poorly differentiated adenocarcinoma. The patient underwent low anterior resection with primary anastomosis. TNM staging was T3N1M0. Due to lymph node involvement, he subsequently received 3 cycles of 5-FU/Leucovorin and radiotherapy. Twenty months after the original operation, patient presented with complaint of left flank pain. His BUN and creatinine were 17 mg/dL (normal range, 7–18) and 1.6 mg/dL (normal range, 0.8–1.4) respectively. Urine analysis and CEA level were normal. CEA. Follow up CT scan revealed left sided hydronephrosis and hydroureter with no evidence of recurrence. Cystoscopy did not indicate any abnormality in the bladder. Retrograde ureteropyelography demonstrated abrupt cut off the injected contrast at the L4 level. A ureteral neoplasm was suspected, and so a left nephroureterectomy was performed. Macroscopic examination of the resected specimen revealed a tumor growth infiltrating the lumen of the ureter. Histopathology of the mass revealed a mucin producing adenocarcinoma involving the mucosal side of the ureter (Fig. 1). Subsequent immunohistochemical staining revealed: positive for cytokeratin 20 (CK 20), negative for cytokeratin 7 (CK 7) and markedly positive CEA. This pattern of staining strongly suggests an intraluminal ureter metastasis from the rectal cancer. Ureter metastasis in resected colorectal cancer indicates advanced disease and suggest poor prognosis. Its presentation as hydronephrosis should be taken as an early indicator of recurrent disease.[figure 1]



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#### Gossypiboma: An Unusual Cause of Gastric Outlet Obstruction Diagnosed by Endoscopy

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**Purpose:** A gossypiboma, or retained surgical sponge is an uncommon surgical complication. Imaging plays a vital role in identifying retained foreign objects. To the best of our knowledge, it has been rarely reported for gossypiboma to cause gastric outlet obstruction. We are reporting a case of gastric outlet obstruction caused by gossypiboma and diagnosed primarily by upper GI endoscopy.

**Results:** A 40-year-old man presented with upper abdominal pain and persistent vomiting for three days prior to admission. The pain was epigastric, non radiating and without any aggravating or relieving factors. He denied history of weight loss, melena or hematemesis. He had a past history of cholecystectomy done abroad 3 years ago. His general physical examination was unremarkable. Abdominal examination revealed a healed right subcostal scar of open cholecystectomy. On palpation, there was an intra-abdominal

firm mass in the right hypochondrium. His hemogram, biochemical parameters, chest x-ray films were normal. After informed consent and overnight fasting, an upper GI endoscopy revealed stomach partially filled with fluids and food particles. Examination was not completed because of fear of aspiration. On repeat endoscopy after a longer fasting period, a fixed foreign body in the antrum obstructing the pylorus was seen. The foreign body had an appearance of woven fiber; a few fibers were removed using biopsy forceps, which suggested a surgical sponge. A contrast-enhanced CT scan of the abdomen revealed a foreign body with radiopaque segment in the proximal duodenum and pylorus with local peritonitis causing gastric outlet obstruction and hyperdistension of the stomach with some free fluid in the pelvis. There was no free air seen. The patient underwent surgical exploration, which confirmed the diagnosis. The sponge was removed, and the fistulous communication was repaired.

**Conclusion:** Although gossypiboma is rarely seen in routine clinical practice, it should be considered in the differential diagnosis of acute mechanical gastrointestinal obstruction in patients who underwent laparotomy in the past. Early recognition of this condition may prompt appropriate investigation and treatment which may reduce morbidity and mortality. The best known approach in the prevention of this condition is meticulous counting of radiopaque surgical material in addition to a thorough evaluation of surgical site at the end of operation.

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#### Diffuse Hemangiomatosis of Colon, Liver and Skin

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**Purpose:** A 58 yr old man came for routine colonoscopy screening. He had no history of gastrointestinal bleeding. Prior tests for fecal occult blood were negative. His past medical history was significant for resection of giant cavernous hemangioma of the left lobe of liver, 10 year ago and multiple residual hemangiomas in the right hepatic lobe. Physical exam revealed multiple cherry red vascular blebs on the back and upper chest, which blanch with pressure. Colonoscopy showed multiple, red colored vascular blebs, seen in the cecum and the adjacent ascending colon. None of the lesions showed active bleeding. The patient demonstrated multiple hemangiomas, involving the colon, liver and skin. At 1 year follow up, the patient continues to remain asymptomatic with no gastrointestinal bleeding or increase in size of liver hemangiomas. To our knowledge, there is no previous case report of multi-organ involvement by hemangiomas.

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#### Atresia of Inferior Vena Cava Presenting as Retro-Peritoneal Masses

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**Purpose:** A 52 yr old white male was referred to GI clinic with complaints of chronic diarrhea, weight loss and abdominal pain for last 3–4 months. Patient had 2–3 bowel movements/day with variable consistency of the stools. No history of hematochezia was present. He had been complaining of sharp, tearing pain in the lower abdomen, radiating to both groins, exacerbated by movement and relieved by sitting. There was no history of fever or night sweats. Physical exam revealed soft, non-tender abdomen with no inguinal or testicular swelling. No inguinal lymphadenopathy was appreciated. Extremities did not reveal any pedal edema. Colonoscopy revealed edematous rectal folds without erosions, ulcers, polyps, or arteriovenous malformations. Biopsy of colonic mucosa showed mild non-specific chronic inflammation of lamina propria and scattered lymphoid aggregates. Testicular ultrasound revealed bilateral varicocele and no testicular pathology. The CT scan of the abdomen showed absence of inferior vena cava; there were multiple collaterals, which appear as soft tissue densities, initially thought to be retro-peritoneal masses. The patient subsequently had a veno-gram, which confirmed absence

of the inferior vena cava with multiple dilated retro-peritoneal collateral vessels. Patient was started on as needed regimen of antispasmodic agents and his weight has improved at 8 months follow up.

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#### Gastric Perforation Due to a Trichobezoar in a Normal Healthy Woman

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**Purpose:** We report a case of a 28-year-old female who presented to emergency department with excruciating epigastric pain that started after she felt a pop in her stomach. The pain was stabbing in nature and associated with feeling of nausea. Prior to this episode, she reported history of intermittent abdominal pain for a period of few months. Her past history was unremarkable, but her mother and husband reported later that they had stopped her from pulling and eating her own hair. She was married, had 2 children and gave no history of any mental illness. A physical examination revealed guarding and rigidity in the epigastric region. Abdominal computed tomography showed free air under the diaphragm (blue arrow), a break in the anterior gastric wall (green arrow) and a large heterogeneous mass in the stomach (yellow arrow) in Figure 1. An initial diagnosis of foreign body/bezoar with perforated ulcer was made. Patient underwent emergent laparotomy which revealed a large trichobezoar (Fig. 2) and a perforation on the anterior wall of the stomach. The bezoar was extracted through an anterior longitudinal gastrotomy. Both the gastrotomy and the perforation were then sutured with regional omental patch. The postoperative period was uneventful. Trichobezoar is a rare diagnosis. Our case is unique as the patient described is a healthy woman with no psychiatric or surgical history. Vague, low grade abdominal pain is a common complaint and clinicians may tend to overlook it. This



case emphasizes need for thorough work up in cases of vague unrelenting abdominal pain.[figure1][figure2]

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#### Inferior Pancreaticoduodenal Artery Pseudoaneurysm: A Rare Cause of Massive GI Hemorrhage

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**Purpose:** A 60-year-old caucasian female with rectal adenocarcinoma (T4 N1 M1) underwent lower anterior resection and segmental ileum resection and 28 cycles of pelvic radiation therapy. One month after the completion of XRT, she was admitted to the Intensive Care Unit for tachycardia and hypotension after an episode of hematemesis. She admitted to having dark stools over the past 3–4 weeks. Hgb on admission was 8.5 gm/dl and she was adequately volume resuscitated with IV fluids and packed red blood cell transfusions. An emergent EGD and Colonoscopy failed to reveal any active sources of bleeding. The patient continued to have melena, and was soon passing BRBPR and had 2 more episodes of hematemesis with bright red blood clots. Her Hgb dropped to 5.5 gm/dl. She then underwent a tagged RBC study with Tc-99m and which revealed a faint area of radiotracer in the left upper quadrant region. A subsequent mesenteric angiogram showed an Inferior Pancreaticoduodenal artery (IPDA) pseudoaneurysm (Fig. 1) and active bleeding into the bowel wall (Fig. 2) which was embolized using microcoils, and post-embolization angiograms showed complete occlusion



of the source of bleeding. The patient did not have any further episodes of bleeding and her Hgb remained stable for the rest of her hospital stay. IPDA pseudoaneurysm is a very rare cause of GI bleeding and is usually a complication of acute or chronic pancreatitis due to auto-digestion of arterial walls from the release of pancreatic enzymes. Other reported causes of visceral artery pseudoaneurysms are inflammation, trauma, neoplasms, or invasive surgical procedures. Aneurysmal rupture can occur into the gut or the peritoneum and can have devastating results if emergent intervention is not done.[figure1][figure2]

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#### Neutropenic Enterocolitis: An Unusual Complication of Hepatitis C Virus Combination Therapy

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**Purpose:** A 53-year-old Caucasian female with known HCV infection was referred for treatment at our institution. She had no history of alcohol intake or other co-morbid conditions. Initial physical exam, and laboratory evaluation including WBC count, chemistries and coagulation parameters, was unremarkable. HCV genotype 1 A, viral load of 427,883 IU/ml and liver biopsy grade 3, stage 4 disease were noted on pre-treatment evaluation. She was started on the standard combination therapy with Pegylated Interferon 180 µg weekly and ribavirin 1200 mg daily. After 12 weeks of starting treatment, she presented with a one week history of fever (103°F), and progressively increasing right lower quadrant cramping abdominal pain. Physical examination revealed a febrile patient with severe tenderness and voluntary guarding over the right lower quadrant of the abdomen. Her labs on admission showed a total WBC count 1100/cmm, Absolute Neutrophil Count (ANC) 550/cmm, platelet count 57000/cmm, and normal liver function tests. CT abdomen revealed bowel wall thickening involving the cecum with dilation (figure) without any evidence of intramural air. Stool studies were negative for leucocytes and Clostridium difficile toxin. In view of her neutropenia, clinical presentation, absence of hypotension, and imaging findings, a diagnosis of neutropenic enterocolitis was made. She responded well to empiric broad spectrum antibiotics, supportive treatment, and G-CSF (Filgrastim) and was discharged home after 10 days of inpatient treatment. Neutropenic enterocolitis is a well known complication of intensive chemotherapy for various malignancies, but has not been reported with the neutropenia associated with HCV combination therapy, which is considered to be well tolerated by most patients. Clinicians should maintain a high index of suspicion for any signs of infection in cirrhotic patients on HCV therapy as the physiologic alterations in bowel wall permeability and neutropenia can act synergistically in causing a serious bacterial infection.[figure1]



### Sigmoid Endometriosis Diagnosed by Endoscopic Ultrasound Fine Needle Aspiration

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**Purpose:** Diagnostic evaluation of submucosal lesions in the sigmoid colon often requires surgical intervention. The use of endoscopic ultrasound fine needle aspiration (EUS-FNA) is an accepted method for investigation of submucosal lesions in the lumen of the GI tract. This case illustrates the value of EUS-FNA in a submucosal sigmoid colon lesion.

A 36-year-old female presented with one month of left lower quadrant abdominal pain. Her past medical history was only significant for depression. There was no fever, constipation, diarrhea, or rectal bleeding associated with the pain. Abdominal exam revealed tenderness in the left lower quadrant without mass. A contrasted CT scan showed fatty mesenteric stranding around the left ovary and sigmoid colon. Pelvic exam and pelvic ultrasound were unremarkable. She was treated with antibiotics for presumed diverticulitis. Colonoscopy performed six weeks later showed submucosal nodules in the sigmoid colon, 20 cm from the anal verge. The nodules were smooth and not mobile. Biopsies showed normal colonic mucosa.

EUS revealed a 20×23 mm nodular hypoechoic mass that involved the muscularis propria of the sigmoid colon. There was a transmural irregular extension of this mass into the pericolonic tissue. EUS-FNA was performed with 3 passes into the mass for cytology. The cytological studies revealed reactive appearing glandular epithelial cells with no evidence of goblet cells. There were focal hemosiderin-laden macrophages present. Immunohistochemical studies were performed on the tissue and identified the epithelium to be cytokeratin 7 positive and cytokeratin 20 negative. Endometrial stromal cells present were CD 10 positive and scattered histiocytes were KP-1 positive. The cytomorphology of the specimen and immunohistochemical profile was diagnostic of endometriosis.

Diagnosis of colonic mural endometriosis is challenging, and this case illustrates the clinical utility for EUS-FNA of submucosal lesions in the sigmoid colon.[figure1]



### EWS-CREB 1: A Novel Variant Gene Fusion Transcript in Clear Cell Sarcoma of the Ileum

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**Purpose:** Introduction: Clear cell sarcoma (CCS) is a rare malignant soft tissue neoplasm that commonly afflicts tendons and aponeuroses in young

adults. Primary CCS of digestive tract is exceedingly rare and only three cases of ileum involvement are reported thus far. We hereby report a patient with CCS of the ileum presenting with abdominal pain and fever.

**Case Report:** A 40 year old African American woman with a history of appendectomy and cholecystectomy, presented with a two day history of lower quadrant abdominal pain and fever. No nausea, vomiting, change in bowel movements, burning micturition or vaginal discharge was reported. Physical exam revealed a fever of 100.7 F, bilateral lower abdominal and cervical motion tenderness. Laboratory data revealed leucocytosis, a negative urinalysis and pregnancy tests. Pelvic ultrasound showed a 7×7×4 cm mixed echogenic complex mass in the left adnexa. After 72 hours of empiric antibiotics for pelvic inflammatory disease, abdominal pain worsened and fever persisted. CT scan of the abdomen showed a 6 cm soft tissue mass engulfing the ileum. The patient underwent exploratory laparotomy with small bowel resection and anastomosis. Surgery revealed a 9.5 × 9.0 × 5.0 cm mass arising from the terminal ileum. The mass was focally ulcerated and infiltrating into the mesentery and the bladder. Pathology reported an epithelioid neoplasm, with small, oval nuclei surrounded by abundant clear cytoplasm and well defined cell membranes. On immunohistochemical examination, tumor cells were strongly and diffusely immunoreactive for S-100 while are negative for melanocytic markers (HMB45, A103) and gastro intestinal stromal tumor (GIST) markers (CD117 and CD34). Reverse transcription polymerase chain reaction analysis performed on paraffin embedded tissue showed EWS-CREB 1 rearrangement, indicating presence of variant t (12; 22) translocation of clear cell sarcoma. Follow up CT scan of the abdomen showed hepatic lesions, histologically consistent with CCS. The patient was started on palliative chemotherapy.

**Discussion:** Cytogenetics and KIT tyrosine kinase stains have a central role in the diagnosis of this highly malignant tumor which can be mistakenly diagnosed as GIST or a melanoma. The outcome of metastatic CCS is dismal despite aggressive surgery and adjuvant therapy.

### Intestinal Spirochetosis: A Cause of Symptoms Resembling Irritable Bowel Syndrome

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**Purpose:** Intestinal spirochetosis (IS) is an uncommon, but treatable cause of gastrointestinal symptoms that often resemble irritable bowel syndrome (IBS). We report a case of IS in a homosexual male presenting with chronic watery diarrhea.

A 25 year old homosexual male of Asian origin presented with an eight-year history of watery diarrhea. He denied rectal bleeding, abdominal pain and weight loss. Physical examination was unremarkable. Biochemical and hematological parameters were normal. Stool examination did not reveal conventional pathogens. No gross abnormalities were noted on colonoscopy. Hematoxylin and eosin (H &E) stained slides of colonic mucosal biopsy specimens revealed a focally prominent surface epithelial brush border with basophilic microorganisms adherent to the epithelial surface, suggestive of IS. The diagnosis was confirmed with Steiner silver stain, which highlighted surface microorganisms. A seven day course of oral metronidazole was offered as therapy for IS.

IS is an uncommon clinical entity in North America, with an estimated prevalence of 2.5% to 6.5%. Higher prevalence rates (11.4 to 64.3%) have been observed in developing countries, in homosexuals and HIV-infected individuals. Colonization of the colonic mucosa by various species of spirochetes, including *Brachyspira aalborgi* and *Serpulina pilosicoli*, is almost an incidental finding in an asymptomatic patient. Spirochetal invasion of the colonic epithelium, resulting in epithelial changes and inflammatory infiltrate in the lamina propria, is associated with symptoms. However, in homosexual men, regardless of HIV status, symptoms may be present in the absence of epithelial invasion. Persistent diarrhea, abdominal pain or constipation occur either

alone or in combination, often resembling IBS. The diagnosis of IS is suspected on H & E staining of colonic mucosal specimens, and confirmed by silver stains, immunohistochemistry or electron microscopy. Due to patchy distribution of spirochetes, multiple site colonic biopsies are recommended for a definitive diagnosis. Of the several regimens proposed, metronidazole seems to be superior in eradicating spirochetes from the intestine.

In conclusion, IS should be considered as a differential diagnosis in patients with IBS-like symptoms, with an otherwise grossly normal-appearing colonic mucosa. Metronidazole should be offered as first-line therapy for the treatment of IS.

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### **Recto-Sigmoid Colon Perforation during Retroflexion in a Patient with Rectal Prolapse: Is This a Safe Practice**

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**Purpose:** Colonic perforation has been well described in the literature as a known complication of colonoscopy, a commonly performed procedure. The perforation risk in colonoscopy has been quoted over a wide range. The rectum is generally felt to be an area of low risk to perforation. We present a case of a 70 year-old gentleman with recto-sigmoid colon perforation occurring during colonoscopy upon retroflexion in the rectum. To our knowledge perforation experienced during retroflexion has not been reported. Interestingly, this patient had prolapse of the rectal mucosa identified on digital rectal examination prior to his colonoscopy. Spontaneous perforation of the recto-sigmoid colon with evisceration of the small bowel in patients with rectal prolapse have been reported.

**Results:** Mr. R. is a 70 year old man referred for a screening colonoscopy. His medical history included a new diagnosis of prostate cancer. General surgery had recently seen the patient for evaluation of suspected rectal prolapse. Prior to insertion of the colonoscope, a rectal exam was performed. There was evidence of rectal prolapse with approximately two centimeters of rectal mucosa extending beyond the anal sphincter along with external hemorrhoids. The colonoscopy was performed to the cecum without complication. The entire colonic mucosa appeared normal without evidence of diverticulosis, stricture, or polyps. Upon retroflexing in the rectum a perforation occurred. The perforation was suspected to be at the recto-sigmoid junction after noting blood approximately 15 cm from the anus. The patient did not complain of any pain and had no abdominal distention, guarding, or rebound tenderness on examination. Upright abdominal film was obtained and showed a small amount of free air. Surgery evaluated the patient immediately, and he was started on antibiotics. He was taken to the operating room and underwent rigid sigmoidoscopy under anesthesia. This did not reveal the perforation so an open laparotomy through a small 4–5 cm incision below the umbilicus was performed. The surgeons identified the mucosal tear, and he underwent of primary repair of 1–2 cm perforation just above the peritoneal reflexion.

**Conclusion:** We hypothesize that rectal prolapse may be a contraindication to retroflexion in the rectum in patients undergoing colonoscopy.

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### **Watermelon Colon: Can This Be an SLE Flare-Up?**

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**Purpose:** A 69-year-old Caucasian female with past medical history of SLE presented with a two-month history of diffuse abdominal pain, occasional nausea, vomiting, bloody stools and uncontrolled diarrhea. She denied any recent travel, change in medications, exposure to contaminated food or water, and fevers or chills. Her symptoms initially responded to over the counter

medications, but she was now having severe diarrhea up to 10 times a day associated with abdominal cramping and bloating. She was on maintenance steroid therapy for her SLE and her last flare-up was several years ago. Physical exam was significant for diffuse abdominal tenderness with no voluntary guarding or organomegaly. Bowel sounds were hyperactive, and no skin lesions or lymphadenopathy were appreciated. Initial labs including CBC, chemistries, LFTs, and thyroid function tests were unremarkable. Stool studies were negative for C. Difficile, ova and parasites, and leukocytes. The patient underwent an elective EGD that showed mild erosive gastritis, and a Colonoscopy revealed extensive, reddish, watermelon-like linear vascular lesions throughout her entire colon extending up to the ileocecal junction, that had the appearance of “Watermelon Colon”. Biopsies confirmed the vascular nature of these lesions and had features of colitis in certain regions. The patient was started on high-dose oral steroids and her symptoms slowly started to resolve. “Watermelon Colon” is an extremely rare endoscopic diagnosis and very few cases have been reported in the literature. Prior reported cases were seen in association with scleroderma or the CREST syndrome and involved focal areas of the colon or the rectum. Only one case describes this entity involving the entire colon, with cecal sparing, seen with a protein-losing enteropathy. Our case is unique in its association with SLE and involving the entire colon, including the cecum. Vasculitis is one of the hallmarks of SLE and it is well-known to involve the GI tract causing erythematous lesions, ulcers, ischemia, infarction, perforation, or inflammatory bowel disease. It is possible that our patient had a flare-up of SLE that manifested as the Watermelon Colon. Various treatment modalities have been proposed for such vascular lesions involving the stomach (Watermelon Stomach) and the colon and include Argon Plasma Coagulation, sclerotherapy, laser photoablation and endoscopic cryotherapy.

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### **Cola Dissolution Therapy in Gastric Bezoar**

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**Purpose:** Bezoars are concretions of indigestible material that coalesce usually in the stomach. In this report, we wished to address one treatment modality for this often vexing clinical problem.

**Methods:** A 90-year-old male was admitted to the hospital because of abdominal distention, vomiting, and increased colostomy output. The patient had a history of dementia and resided in a foster home. Physical examination revealed an alert but demented elderly male with stable vital signs. Abdomen was distended with normoactive bowel sounds. Right lower quadrant tenderness was present. The patient had been recently admitted with similar symptoms. Evaluation at that time with plain abdominal films had revealed a distended stomach with a large amount of food. The patient then improved spontaneously and was returned home without further testing or treatment.

Upon admission, abdominal CT scan was suggestive of gastric outlet obstruction. Esophagogastroduodenoscopy (EGD) showed a large bezoar occupying most of the gastric lumen. Several gastric ulcers were seen in the antrum, away from the pylorus. There was no evidence of gastric outlet obstruction. Given the patient's age and comorbidities, his family wished to avoid surgery. Papain use was ruled out because of side effects, and cellulase was not available. Therefore it was decided to use gastric instillation of cola (Coca-Cola®) in an attempt to dissolve the bezoar.

**Results:** Following intragastric lavage with cola for 12 hours, EGD showed persistence of the bezoar. However, the patient was now able to keep liquids down. He was discharged to home on proton pump inhibitor therapy, with instructions to drink 2 cans of cola daily and to follow a liquid diet. Follow-up EGD 2 months later revealed complete disappearance of the bezoar and healing of the gastric ulcers.



**Conclusion:** After a thorough literature review, we were able to retrieve only a paucity of articles regarding cola dissolution therapy for gastric bezoars. Three such reports describe successful dissolution, with varying methodologies used. To the best of our knowledge, our report is the first of cola dissolution therapy in the United States. We propose that cola dissolution therapy is a valid option for dealing with gastric bezoars. It is anecdotally efficacious and carries virtually no side-effects. It should be offered to patients as part of the therapeutic armamentarium. However, this therapy has yet to be subjected to a randomized controlled trial, and is probably best reserved for the non-surgical candidate.

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#### **Gallbladder Remnant: Rare Cause of Abdominal Pain Post Cholecystectomy**

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**Purpose:** Thirty-six year old male presented to gastroenterology clinic with sharp right upper quadrant pain for a month radiating to his back. He also described nausea but denied emesis, dysphagia, change in bowel habits, jaundice, fever, chills, sweats and weight loss. His past medical history was significant for acute cholecystitis in November 2003 requiring an urgent cholecystectomy.

Physical exam was remarkable for minimal tenderness in right upper quadrant upon palpation. Vital signs and labs were normal. Computed Tomography (CT) scan was normal. Ultrasound report commented on a 1.3 cm simple liver cyst and a 1.2 cm cystic structure containing a 6.7 mm calcification in the location of the gallbladder fossa.

Gastroenterology recommended evaluation with a Magnetic Resonance Cholangiopancreatography (MRCP), which revealed a cystic duct remnant with small stones. Endoscopic Retrograde Cholangiopancreatography (ERCP) was performed to confirm MRCP findings prior to surgical exploration and resection. ERCP revealed normal common bile ducts, no filling defects, and a long cystic duct with an early take off from the common bile duct. As contrast continued to be injected, a structure suggestive of a gallbladder remnant continued to fill. Gallbladder remnant was identified and general surgery planned a surgical resection, which revealed a gallbladder remnant with an impacted stone (Fig. 1).

Retained gallbladder remnant is a rare complication of cholecystectomy and is more common in the era of laparoscopic cholecystectomy. Symptoms can occur from new stones forming in remnant or from harboring residual stones. Patients usually present months to years after initial surgery. Diagnosis is difficult to make and requires MRCP or ERCP. Treatment in all cases requires surgical excision with either laparoscopic or open procedure.

In summary, gall bladder remnant is a rare complication of cholecystectomy and reported in the literature in a number of case series and case reports. Gastroenterologists should be aware of this diagnosis because it is difficult to make without a high index of suspicion.[figure1]



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#### **Gastric Polyps Causing Intermittent Gastric Outlet Obstruction**

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**Purpose:** A 40-year-old Caucasian male with a history of GERD and Osgood-Schlatter disease presented with acute-onset of abdominal bloating, nausea and vomiting for one month. His daily symptoms were worse at night, usually resolving by the next morning. He denied any worsening heartburn, weight loss, appetite changes, dietary changes or modification of bowel habits. He had been on long-term proton-pump inhibitor therapy for GERD and was taking NSAIDs for osteochondritis. Elective gastroscopy showed multiple large gastric polyps occupying the gastric fundus and body. Two of these polyps were pedunculated and were prolapsing into the pyloric channel, presumably causing intermittent gastric outlet obstruction. We endoscopically removed two 3.5 cm hyperplastic polyps by snare technique. The patient's symptoms completely resolved following this intervention. Proton-pump inhibitors are widely used in clinical practice and are associated with an increased incidence of hyperplastic gastric polyps via stimulation of enterochromaffin-like cells. Gastric polyps causing gastric outlet obstruction should be considered in the differential diagnoses of abdominal distention.[figure1][figure2]



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#### **Fleeting Hepatomegaly Due to Glycogenic Hepatopathy in Uncontrolled Type I Diabetes Mellitus**

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Medical Center, Chicago, IL and Pathology, Rush University Medical Center, Chicago, IL.

**Purpose:** Glycogenic Hepatopathy (GH) is an under-recognized pathologic overloading of hepatocytes with glycogen in patients with poorly controlled type I diabetes mellitus. We present a case of GH and discuss its clinical presentation, diagnosis, and management.

**Case presentation:** An 18-year-old woman with Type I diabetes mellitus since age 5 was admitted via the emergency department for worsening nausea, vomiting, right upper quadrant pain, and increased abdominal girth. Physical examination revealed tender hepatomegaly 8 cm below the right costal margin. Laboratory data revealed an AST of 170 U/L, ALT 120 U/L, alkaline phosphatase 181 U/L, total bilirubin 0.8 mg/dl, HbA1C 12.5%. Subsequent laboratory screening for viral hepatitis and autoimmune hepatitis were negative. The patient denied alcohol use. A computed tomography scan of the abdomen revealed significant hepatomegaly without other abnormalities. An abdominal ultrasound revealed a liver measuring 17.5 cm in length with increased echogenic parenchyma suggestive of fatty infiltration. The hepatic vascular indices were normal. A trans-jugular liver biopsy revealed swollen hepatocytes, pale cytoplasm, and numerous glycogenated nuclei. A periodic acid-Schiff stain with and without diastase digestion demonstrated extensive glycogen deposition confirming the diagnosis of GH. Fibrosis, steatosis, and inflammation were absent. With aggressive glycemic control, the patient's abdominal pain, girth, and liver function abnormalities improved and the patient was discharged. Subsequent follow-up laboratory data revealed improved HbA1C and normal liver function tests.

**Discussion:** GH is a complication of uncontrolled type I diabetes mellitus. Patients often present with liver function test abnormalities and abdominal pain, hepatomegaly, nausea, or vomiting. Glycogen is not toxic to hepatocytes and the elevation in liver enzymes is likely secondary to leakage from hepatocyte injury rather than cell death. Many physicians often mistake GH for fatty liver disease. Imaging and laboratory testing cannot effectively distinguish between these two entities. The diagnosis is made by liver biopsy which reveals marked glycogen accumulation in hepatocytes. Unlike steatosis, GH is not known to progress to cirrhosis. Management strategies for GH focus primarily on achieving strict glycemic control.

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#### Severe Pulmonary Hypertension in Whipple's Disease

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**Purpose:** A 49 year-old Caucasian male presented with 6 weeks of dyspnea, increased abdominal girth, diarrhea and lower extremity edema. Auscultation disclosed normal heart sounds but decreased breath sounds at the lung bases. His abdomen was protuberant without masses or organomegaly and he had bilateral lower extremity edema.

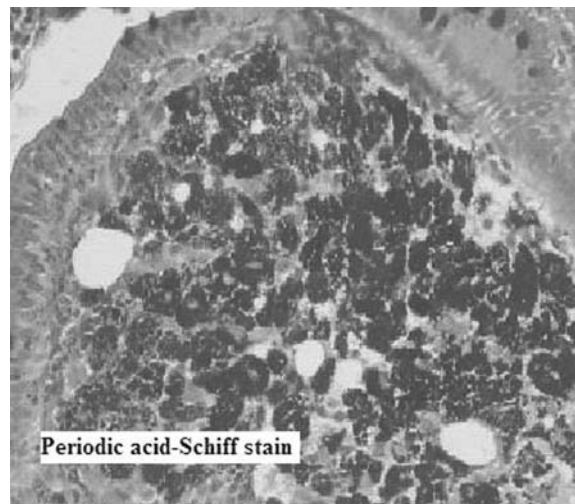
His albumin level was 1.8 g/dL despite normal liver function tests. Imaging studies of his chest and abdomen showed large bilateral pleural effusions, a small pericardial effusion, ascites and edematous loops of bowel. Echocardiographic evaluation revealed a normal ejection fraction and no valvulopathies. However, elevated right ventricular pressures led to a cardiac catheterization which disclosed a pulmonary artery pressure of 90 mmHg, consistent with severe pulmonary hypertension. The presence of microcytic anemia (hemoglobin of 8.2 g/dL), prompted upper endoscopic evaluation, which disclosed mild duodenitis. Small bowel biopsies demonstrated acute inflammation and numerous Periodic acid-Schiff stained macrophages in the lamina propria (Fig. 1). PCR confirmatory studies were positive for *Tropheryma whipplei*. Antibiotic therapy led to resolution of his symptoms and normalization of the pulmonary artery pressures over the following 16 weeks.

**Discussion:** Whipple's disease is a rare systemic disorder characterized by arthralgias, weight loss, diarrhea, and abdominal pain. Pulmonary involvement occurs in 30 to 40% of cases, usually as pleural effusions, pulmonary

infiltrates or mediastinal adenopathy. Pulmonary hypertension, however, is an infrequent finding.

To the best of our knowledge, only three cases of severe pulmonary hypertension in Whipple's disease have been previously reported in the English literature. Two of those cases involved patients with valvular heart disease, probably from blood-culture negative *T. whipplei* endocarditis.

In our case, we suspected a causal relationship between Whipple's disease and pulmonary hypertension, as evidenced by resolution of the latter following antibiotic therapy. Direct involvement of the pulmonary vascular bed by *T. whipplei* is therefore assumed.[figure1]



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#### Preventing Recurrent Gastro-Gastric Stricture as a Complication of Roux-en-Y Gastric Bypass Surgery

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**Purpose:** Balloon dilation as a treatment for post-surgical anastomotic strictures is minimally invasive and relatively safe. The benefit of through-the-scope dilators has a reported long-term improvement of 48 to 66%. Placement of a temporary stent is an option that we reported for benign esophageal stricture. This is a patient with gastro-gastric anastomotic stricture which was treated by injecting triamcinolone (TRIAM) into the stricture, using a protocol described for esophageal strictures, after multiple balloon dilations provided short term relief.

**Case:** A 40 year old female, 4 years after Roux-en-Y gastric bypass surgery, was transferred following extensive small intestine and right colon resection following a small bowel volvulus with infarction of the entire jejunum, ileum, and right colon. A duodenocolostomy was planned as a bridge to transplantation, but was not feasible due to inflammation. Therefore the distal duodenum was closed primarily; EEA gastrogastrostomy with distal decompressive tube gastrostomy was performed. At 1 month she had nausea and vomiting. At EGD there was a high grade stricture of the gastro-gastric anastomosis. Under fluoroscopy, the anastomosis was dilated with through-the-scope balloon dilators. Five additional dilations provided temporary relief. Due to nausea and vomiting, a seventh EGD at day 50 revealed a residual high grade stricture. During this session, the stricture was dilated with a balloon dilator to 12 mm and then the stricture was injected circumferentially 5 times with 10 mg of TRIAM. Due to the absence of recurrent

symptoms she did not require repeat dilation for 3 months; EGD prior to transplantation revealed a patent gastro-gastric anastomosis. At 3 months after small intestinal transplantation, she was clinically doing well.

**Discussion:** This case report demonstrates that injection of TRIAM into an anastomotic stricture following GI surgery improves long term efficacy of dilation. TRIAM is preferable to cortisol, as it is locally active for 4 weeks and is more potent at degradation of collagen fibrils. This novel approach appears to be an effective method for managing an unusual complication of gastric bypass surgery without the risk of perforation due to repetitive endoscopic dilations.

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#### An Atypical Presentation of Hepatocellular Carcinoma

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**Purpose:** This is a 69-year-old Laotian male with a history of prior partial hepatic resection for unknown reasons, who is admitted to the university hospital for a palpable right upper quadrant mass causing RUQ pain, 8/10 in severity, and radiating into the back. No factors seem to affect the pain negatively or positively. Four years ago, he noticed the appearance of a right upper quadrant mass, which did not cause him significant pain until three weeks prior to presentation. One week prior to presentation, the patient had a CT scan done showing a 12.5 × 11.5 cm multilocular liver mass. The mass appeared mostly cystic with multiple loculations and thick intervening septa. There was an inferior vena cava thrombus and multiple pulmonary emboli. Patient's review of systems was negative. The patient noted mild weight loss, which he cannot quantify. He reports bilateral ankle swelling present for the last two days, and frequent drenching night sweats. He moved to the United States in 1981 from Laos. Physical exam was remarkable for an afebrile patient with a grapefruit-size, right upper quadrant, tender, firm mass, a large surgical scar over the right upper quadrant, and 2+ pitting edema bilaterally. Labs were notable of a WBC of 15,000, Hct 29, Plts 251, and Eosinophils 25.1%. Basic metabolic panel was within normal limits. LFTs were notable for an Alkaline Phosphatase of 502, AST 48, ALT 28, TP 8.7, Alb 2.8, TB 0.8, GGT 334. Hepatitis A, B, and C were negative. AFP was 4, Alpha-1-AT, ANA, LKM1, ASMA, Stool O&P × 3 were all negative. His iron percent saturation was 22%. E. histolytica and Echinococcus studies were negative. Toxocara IgG was positive at 4.1. Serum Fasciola hepatica, Clonorchis sinensis, and echinococcal serologies were sent to the CDC during this hospital course. The patient, due to his multiple pulmonary emboli and IVC thrombus was started on heparin and bridged to coumadin. The differential diagnosis included the infectious etiologies tested for, biliary cystadenocarcinoma, and hepatocellular carcinoma. The patient was started on albendazole 400 mg p.o. b.i.d. secondary to the elevated Toxocara IgG. Patient failed to show up for his follow-up appointment, and then presented to another hospital ten days later in PEA. One hour later, he was pronounced dead. At autopsy, it was determined that the solid and cystic mass in his liver was a hepatocellular carcinoma that had occluded the hepatic vein and IVC via direct extension. One must consider HCC in the setting of an apparent infectious etiology of a hepatic mass.

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#### Reactive Thrombocytosis Following Liver Transplant

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**Purpose:** Patient is a 66-year-old white male with past medical history significant for total colectomy due to ulcerative colitis and primary sclerosing cholangitis who underwent DCD orthotopic liver transplantation on April 22, 2007, for primary sclerosing cholangitis. The patient was positive for CMV, and the donor was CMV negative. The patient had a Roux-en-Y choledochojejunostomy for biliary anastomosis. The patient had an uneventful postoperative course, and was discharged within seven days; however,

the patient then began to develop increasing LFTs, GGT, and total bilirubin. On physical exam, vital signs were within normal limits, the patient's chevron scar was well healed, and there were no other physical exam findings. Patient was also noted to have a steadily increasing platelet count. A liver biopsy was done that was consistent with possible biliary obstruction. Multiple imaging studies were done to evaluate for both biliary and vascular obstruction. No obstruction was seen, but there were multiple areas of sludge in the common bile duct as well as a tiny splenic remnant. The patient had a percutaneous drain placed. Since that time, the LFTs gradually returned to normal limits. The patient has a good appetite and good energy levels. He was tolerating all PO and denies diarrhea, nausea, vomiting, chills, fevers, shortness of breath, chest pain, palpitations, headache, blurry vision, dysuria, or polyuria. His platelets, however, continued to climb to a peak of 1.08 million. Prior to transplant, the patient's platelet count was between 300,000 and 400,000. The peripheral smear was significant for Howell-Jolly bodies, target cells and spherocytes. It was felt that the patient was effectively asplenic and had reactive thrombocytosis. Patient was treated with a ten day course of hydroxyurea and platelet count has remained under 500,000.

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#### Anidulafungin Induced Cholestasis Following Liver Transplant

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**Purpose:** Patient is a 56-year-old Caucasian male who is status post liver transplantation on 5/30/06 for chronic hepatitis C, cirrhosis, and concomitant hepatocellular carcinoma. The patient had posttransplant complications including loculated fungal peritonitis with an organized intraabdominal abscess that has required catheter drainage. His fluid grew out *Candida tropicalis* resistant to voriconazole. Anidulafungin was administered at 200 mg for the first dose and then 100 mg once daily each day thereafter. Two weeks after starting this medication, the bilirubin had climbed to 9.1 from 0.6 with a GGT up from 67 to over 2000. The remainder of the patient's labs remained stable including his CBC, coagulation studies and CHEM 14. Patient's vital signs were within normal limits. The physical exam was only significant for a well healed chevron scar and jaundice. While recent liver biopsy findings were suggestive of large duct obstruction, an MRCP did not show any significant extrahepatic duct dilation and ERCP confirmed this finding. It was felt the cholestatic picture was likely secondary to the anidulafungin and it was discontinued. Within two weeks, the bilirubin fell to 2.8 and the GGT dropped to 228. The anidulafungin was restarted due to the severity of the fungal infection. The bilirubin and the GGT again rose, but the drug was continued for two more weeks until the infection was eradicated. Following discontinuation of the anidulafungin, the patient's labs again returned to normal limits. The patient is now over one year out from his transplantation and 9 months out from his infection and continues to do well. Prior to reporting these events to the maker of the drug, there was no evidence reports of elevated bilirubin associated with anidulafungin. Now it is a box warning. In the case of our patient, we were able to successfully treat the *Candida tropicalis* while tolerating the elevated GGT and bilirubin in a newly transplanted patient.

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#### A Case of Ileocecal Tuberculosis Found on Screening Colonoscopy

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**Purpose:** While gastrointestinal tuberculosis is often thought of as a disease of the developing world, clinicians in the United States should not forget to entertain it as a possibility too. Here we present a case of ileocecal TB discovered on a screening colonoscopy.

**Methods:** A 61 year-old female presented for a screening colonoscopy. She had no abdominal pain, no change in bowel habits, and no bleeding. The colonoscopy showed an ileal ulcer 5 cm from the ileocecal valve. The ulcer was biopsied, and histology showed epithelial granulomas with one acid-fast bacillus. The cultures were negative for acid-fast bacilli. The patient denied any known exposure to tuberculosis. The PPD was positive, but the chest x-ray was negative. An HIV test was negative. This was felt to be consistent with gastrointestinal tuberculosis. The patient was referred to TB clinic and was started on a four drug anti-tuberculosis regimen. We performed a literature search to learn more about this disease that is uncommon in our patient population.

**Results:** It is estimated that 50% of the worlds population is infected with TB, and 5% of these patients have gastrointestinal TB. Gastrointestinal TB has been rare in the United States, but its prevalence has been increasing in recent years because of the rise of HIV and the increase of immigration from developing nations. TB can affect the gastrointestinal tract anywhere, but the area around the ileocecal valve is the most commonly affected site. The gut becomes infected by swallowed organisms, which then enter the mucosa and are trapped in the submucosal lymphatic tissue. The most common presenting complaint is abdominal pain. Fever, diarrhea, and anorexia may also be present. Colonoscopy is the initial test of choice and may reveal a deformed ileocecal valve, mucosal nodules, or rounded ulcers surrounded by inflamed mucosa. The definitive diagnosis is made by isolating acid-fast bacilli from a biopsy, either by histology smear, culture, or PCR. Abdominal CT may show wall thickening of the affected bowel. Treatment with a standard anti-tuberculosis regimen should be initiated if there is high suspicion.

**Conclusion:** Gastrointestinal tuberculosis can be a difficult diagnosis to make. However, with the rise in the prevalence of HIV and with a greater mobility of people from at risk-nations, endoscopists and pathologists should be aware and maintain a high index of suspicion for this dangerous yet treatable disease.

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**Hiccups: A Subtle Sign of Gastric Volvulus?**

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**Purpose:** Volvulus is defined as an abnormal twisting of bowel upon itself resulting in luminal obstruction. This often occurs in the small intestine of pediatric patients with malrotation leading to obstruction. It is also seen in the large intestine, most commonly causing obstruction in the cecal and sigmoid regions. Another less common condition is gastric volvulus. Acute gastric volvulus is an emergency and an accurate timely diagnosis is essential. We present two cases of gastric volvulus where a major complaint of both patients was hiccups. These cases are reported to alert physicians to the possibility of hiccups as a subtle but important finding to suggest the diagnosis of gastric volvulus in the appropriate clinical setting. This is important because untreated gastric volvulus can potentially lead to incarceration and mesenteric ischemia with a high mortality.

**Results: Case 1:** A 63 year old man presented with a one week history of nausea, vomiting, abdominal pain and progressively worsening hiccups. Physical exam showed some abdominal distention with mild diffuse tenderness. CT of the abdomen showed a distended, fluid-filled stomach with a twisting pattern consistent with an organoaxial gastric volvulus. Exploratory laparotomy showed a dilated stomach and paraesophageal hernia. Hernia repair was performed and the patient did well after surgery.

**Case 2:** An 89 year old man presented with complaints of epigastric pain, nausea, vomiting, coffee ground emesis, and progressively worsening hiccups. Four months prior, an EGD had shown the presence of a large hiatal hernia. Presenting symptoms and known history of hiatal hernia suggested a possible diagnosis of gastric volvulus. Abdominal CT was consistent with a mesenteroaxial gastric volvulus confirming our clinical diagnosis. The patient was taken to the operating room, and a laparoscopic reduction of his gastric volvulus was performed.

**Conclusion:** Gastric volvulus is an uncommon but potentially devastating condition if not diagnosed in a timely manner. In 1904 Borchardt described the classic triad of epigastric pain, retching and inability to pass a nasogastric tube in patients with a gastric volvulus. In our cases, an interesting finding was the presence of hiccups in both patients. Irritation of the diaphragm by a sliding gastric volvulus or paraesophageal hernia could theoretically trigger hiccups. In the presence of signs and symptoms suggestive of gastric volvulus, it may be appropriate for physicians to inquire about the presence of hiccups while obtaining the patient's history.

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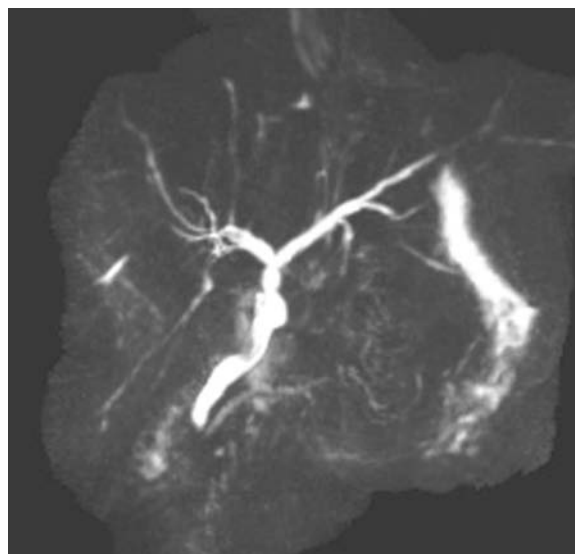
**A Case of Delayed-Onset Cholestasis Due to Lisinopril Use**

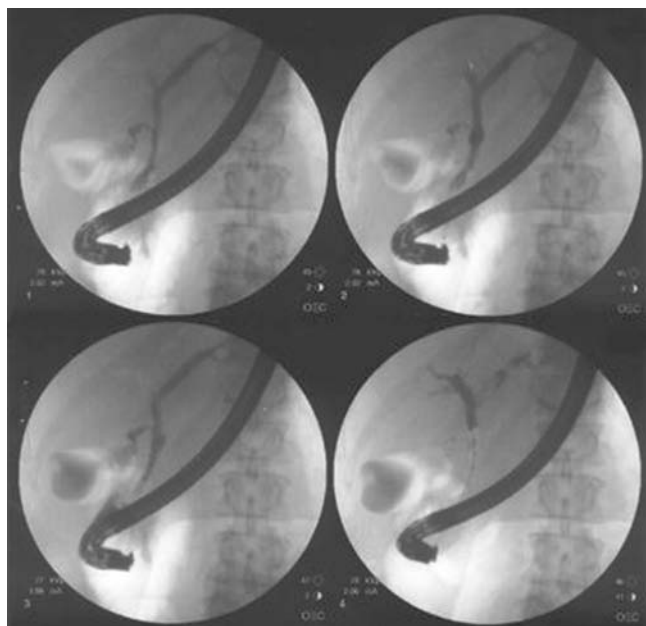
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**Purpose:** A 66-year-old female presented with 1 week-history of painless jaundice. She denied fever or weight loss and reported no recent travel, alcohol use, or dietary exposures. Past medical history was not significant. Chronic prescription medicines included levothyroxine, esomeprazole, sertraline, and lisinopril, which she had taken for 3 years. Liver chemistries 3 years prior were normal. Serum liver testing showed alkaline phosphatase 795, total bilirubin 17.1, direct bilirubin 8.8, ALT 304, AST 392, albumin 4.4, and total protein 6.1. Viral and autoimmune hepatitis serologies were negative.

MRCP showed three areas of stricturing within the common hepatic duct (Fig. 1). ERCP was performed, which revealed an irregular common bile duct and moderate dilation proximally (Fig. 2). Biliary stenting was performed, and pathology was negative for malignancy. The bilirubin continued to rise to a maximum level of 26.3. Liver biopsy was performed and was suggestive of cholestatic hepatitis secondary to drug induced injury. Lisinopril was discontinued, with a slow resolution of jaundice and normalization in liver chemistries over three months. ERCP was repeated for stent removal and cholangiogram revealed a normal biliary tree.

ACE inhibitor-induced hepatotoxicity typically presents within 8 weeks of drug initiation. In this case the patient had been taking lisinopril for over 3 years without clinical signs or symptoms. This case does not follow the typical pattern of presentation and suggests that lisinopril may cause chronic subclinical liver injury, with a delayed onset of symptoms presenting as severe cholestasis. There is a possibility that chronic inflammation may have also involved the extrahepatic biliary tree. This is an atypical case in which identification of drug-induced cholestasis prevented possible life-threatening hepatic injury.[figure1][figure2]





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#### Diverticulosis Presenting as Recurrent Bacteremia

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**Purpose:** We present a case of a 71 year old man with a past medical history of diverticulosis who presented with one month history of dysuria, lethargy and fever.

Work up initially showed multiple organisms in the urine; however his blood cultures in 2 bottles grew proteus mirabilis. The patient was treated with IV antibiotics and after improvement; he was transferred to the geriatric rehabilitation unit. Subsequently, the patient developed multiple episodes of UTI and bacteremia. Urinary obstruction secondary to an enlarged prostate was initially suspected, however, the patient started to report foul smelling urine and pneumaturia. CT scan of the abdomen showed the possibility of a fistula between a diverticulum in the sigmoid colon and the bladder with no evidence of diverticulitis. The patient had no clinical history suggestive of previous episodes of diverticulitis. Colonoscopy was done and malignancy and IBD were ruled out. Cystoscopy confirmed the presence of the fistula. Patient underwent successful surgical treatment.

**Conclusion:** Colovesical fistula (CVF), first described by Cripps in 1888, is caused by various inflammatory or neoplastic processes. Diverticulitis is the most common underlying cause, followed by carcinoma, radiation, Crohn's disease and ruptured appendix. Diverticulosis is a rare but important cause of CVF. In patients with recurrent UTIs and other symptoms of CVF, Diverticulosis should be ruled out.

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#### Twist of Fate: Intestinal Non-Rotation and Intermittent Volvulus in an Adult Treated with Laparoscopic Lysis of Ladd's Bands

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**Purpose:** Intestinal malrotation or non-rotation is well described in infants and children, but rare in adults. Most adults with intestinal malrotation are

asymptomatic, and the anomaly is discovered incidentally. In the rare symptomatic adult with intestinal malrotation or non-rotation, mid-gut volvulus can be life-threatening. We describe an adult with symptomatic intestinal non-rotation treated successfully with laparoscopic lysis of Ladd's bands.

**Methods:** The clinical course of a patient diagnosed with congenital non-rotation is described. She was studied by CT scans, small bowel follow-through x-rays, endoscopy, and obstructive series during symptomatic episodes.

**Results:** A 45 year old female complained of intermittent episodes of severe abdominal pain, associated with nausea, vomiting and abdominal distension, since her teenage years. They would last 45 minutes to several hours, and would spontaneously subside. Severe episodes necessitated emergency room visits, where obstructive series would occasionally reveal small bowel dilation with air-fluid levels. A CT scan revealed that all her colon was on the left side of the abdomen. Her small bowel was on the right side of her abdomen, as seen on CT scan and by small bowel follow-through x-rays. On CT scan, the superior mesenteric artery was on the right side of the superior mesenteric vein, contrary to normal anatomy. The third and fourth portions of the duodenum were entirely anterior to the superior mesenteric artery, rather than posterior to it, and occurred in the right upper quadrant, rather than the left. At laparoscopy, Ladd's bands were seen, as well as a narrow mesenteric pedicle. Ladd's bands were lysed, appendectomy performed, and the non-rotated positions of the small and large bowel were left as is. The patient did well without recurrence of symptoms in follow-up.

**Conclusion:** Symptomatic adult intestinal malrotation or non-rotation is rare, but can be associated with life-threatening mid-gut volvulus and intestinal infarction. Laparoscopic lysis of Ladd's band can successfully treat this rare but potentially life-threatening condition in adults.

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#### This Is the Pits: A Case of Esophageal Foreign Body Impaction

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**Purpose:** The esophagus is the most common location in the gastrointestinal (GI) tract for foreign body impactions and endoscopic removal is the best treatment. While performing endoscopic foreign body removal, it is critical to protect the airway from inadvertent aspiration of saliva and the object during extraction. Indications for tracheal intubation prior to endoscopy include inability to tolerate secretions or finding a radiopaque object within the esophagus. We present the case of a patient able to tolerate secretions after swallowing an apricot pit, whose radiographic film was initially read negative, who during endoscopy was found to have the pit impacted just distal to his upper esophageal sphincter (UES).

**Methods:** A 79-year-old Hispanic male presents five hours after ingesting an apricot pit. The patient initially coughed up pieces of apricot but was unsure if the pit had been expelled. Initially he felt pain and neck fullness but subsequently only experienced odynophagia. On exam, he was afebrile, with normal blood pressure and pulse, chest without crepitus, and soft, nontender abdomen. Labs were unremarkable. A neck soft tissue series was initially read negative. Upon endoscopic esophageal intubation the apricot pit was seen just distal to the UES. The endoscope was withdrawn and the patient intubated for airway protection. The endoscope was reinserted and attempts at removal including use of Roth net, snare, stone extraction basket, alligator forceps, three prong polyp grabber, and ERCP stone extraction balloon were unsuccessful. Airway protection and access were aided by esophageal overtube. After prolonged attempts endoscopy was aborted. Otorhinolaryngology was consulted who decided to remove the pit with a rigid esophagoscope in the Operating Room. The pit was successfully removed under general anesthesia and inflamed, edematous tissue was noted. Review of the initial soft tissue film confirmed the radiopaque pit in the esophagus. Gastrografin study after removal did not demonstrate a perforation. Subsequent upper GI barium esophagram was with-

out obstruction. The patient was discharged without complication two days later.

**Conclusion:** The presence of persistent high esophageal obstruction should be suspected even in the absence of alarm symptoms and despite normal imaging. Our patient is unusual in terms of his benign complaints and normal studies. Endoscopic attempts at removal of high esophageal foreign body impactions are reasonable to attempt as long as adequate airway protection is in place.

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### Severe Systemic Lupus Erythematosus Induced by Antiviral Treatment for Hepatitis C

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**Purpose:** There have been only 9 reported cases in the medical literature of systemic lupus erythematosus (SLE) developing in patients receiving  $\alpha$ -interferon treatment in hepatitis C. We report a case of a 43 year old man who had SLE develop after receiving pegylated  $\alpha$ -interferon and ribavirin for chronic hepatitis C.

**Methods:** He had previously been diagnosed with a non-specific inflammatory arthritis and was commenced on 15 mg prednisone daily with good symptom control. He was found to have an elevated HCV RNA viral load (>800,000 IU) genotype 3 with elevated ALT. He was commenced on treatment with pegylated interferon  $\alpha$ -2a at a dose of 180 micrograms per week and ribavirin 400 mg twice daily. His HCV RNA viral load became undetectable at 12 weeks with normalisation of liver enzymes. However 14 weeks into treatment he presented with a severe flare of arthritis and pleuritis. His interferon and ribavirin were ceased. 4 weeks after discontinuing antiviral treatment he was admitted to hospital with recurrent arthritis and pleuritis.

**Results:** His hospital admission was prolonged and he displayed 8 features of the American College of Rheumatology (ACR) criteria for SLE – notably arthritis, pleuritis, florid discoid rash, anaemia and lymphopenia, oral and aphthous ulceration, glomerulonephritis, the development of high titres of ANA and anti-double stranded DNA antibodies after antiviral therapy. His hospital admission was complicated by life-threatening myocarditis and vasculitis which necessitated admission to an intensive care unit. He was administered pulsed cyclophosphamide, methylprednisolone and intravenous gammaglobulin.

**Conclusion:** He made a slow but complete recovery aided by rehabilitation. Unfortunately his HCV viral load is now detectable and there is evidence of a mild transaminitis consistent with a recurrent flare of hepatitis C viral replication. This case is notable for the clinical severity and nature of multi-organ lupus involvement arising from hepatitis C antiviral therapy.

#### Autoimmune serological progression and clinical events

Dates	Clinical events and ANA levels	Anti ds-DNA (<7 IU/ml)
12/7/05	1:640	0
1/4/06	Interferon and ribavirin commenced	
24/4/06	> 1:2560	2
26/7/06	Interferon and ribavirin discontinued > 1:2560	90
15/8/06	Admission to hospital with severe arthritis and pleuritis > 1:2560	800
19/9/06	Admission to the intensive care unit	
3/1/07	> 1:2560	11

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### Pandisaccharidase and IgA Deficiency Diagnosed in Adulthood

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**Purpose:** A 40 year old Caucasian lady from a rural community near Cairns presented to our gastroenterology clinic for investigation of chronic diarrhoea since infancy. She passed at least 8 bulky stools per day and her bloating and flatulence had been worsening recently. Past medical history was otherwise unremarkable. She was on no medications. Physical examination was normal. Her family history was significant for a deceased brother who had diarrhoea since infancy that had also never been investigated. Her dietary history was notable for avoidance of sugary foods since early childhood.

**Results:** Her faecal fat test was mildly raised. IgA deficiency was noted on blood tests 0.77 (1.24–4.16 g/L). HIV testing and her immunoglobulin subsets apart from IgA were normal. Coeliac serology was negative. She was started on a gluten challenge prior to endoscopy. Upper endoscopy and colonoscopy revealed no macroscopic lesions. Duodenal and colonic light microscopies were completely normal. Evaluation for disaccharidase deficiency revealed pandisaccharidase deficiency (see Table 1). She commenced a lactose free diet which resulted in partial alleviation of symptoms. Capsule endoscopy noted a number of small aphthous ulcers in the proximal and mid small intestine. Abdominal CT scan revealed only mild gas distension of small bowel loops. A repeat endoscopy 6 months later was normal with no abnormalities found on small intestinal light and electron microscopies. Testing of duodenal and jejunal disaccharidases reconfirmed pandisaccharidase deficiency.

**Conclusion:** Special approval was obtained for sacrosidase enzyme replacement. She was commenced on sacrosidase with lactose dietary restriction. Her symptoms resolved within 10 days. This lady is thought to have a congenital sucrose isomaltase deficiency combined with an IgA and acquired lactase deficiency. She has consented for genetic analysis of her blood and intestinal tissue.

#### Results of disaccharidase testing

	Duodenal biopsy 25/9/06	Duodenal biopsy 21/3/07	Jejunal biopsy 21/3/07
Small intestinal enzymes			
Alkaline phosphatase (200–1000 U/g protein)	260	220	630
Isomaltase (38–180 L U/g protein)	8	5	14
Sucrase (26–120 L U/g protein)	2	2	1
Lactase (20–120 L U/g protein)	4	2	9
Maltase (100–400 L U/g protein)	25	22	72
Trehalase (8–50 U/g protein)	–	20	46
Biopsy weight (mg)	8.7	25.2	13.9
Protein (mg/g wet tissue)	36	75	62

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### Gastrointestinal Bleeding in a Patient with Pancreatico-Jejunostomy Diagnosed and Treated with Double-Balloon Endoscopy

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**Purpose:** Diagnosis and therapy of gastrointestinal bleeding in post-surgical patients can be very challenging due to their altered anatomy. We describe a patient who developed massive GI bleeding after a Roux-en-Y procedure and was diagnosed and treated successfully with double-balloon endoscopy (DBE).

**Methods:** Case report.

**Results:** A 50 year old female with history of Roux-en-Y pancreatico-jejunosomy (Puestow procedure) for chronic pancreatitis four years earlier, presented with recurrent massive gastrointestinal bleeding, requiring multiple units of blood transfusions. Standard endoscopies, push enteroscopy, as well as bleeding scans and mesenteric angiography failed to reveal an etiology. An urgent capsule endoscopy study, performed during one of the bleeding episodes, showed blood in the distal small bowel without a clear source. At DBE, the pancreatico-jejunal anastomosis including the remnant of the pancreatic duct openings were clearly seen. Active bleeding ensued about probing the blind end of the jejunal pouch. The bleeding was controlled after injecting epinephrine and the application of two endoscopic clips. Post-procedural angiography revealed a possible minute aneurysm on a branch of the dorsal pancreatic artery in the area of the endoscopic clips. The patient's hemoglobin normalized over the following weeks and no further bleeding occurred at 9 months follow-up.

**Conclusion:** In conclusion, we are presenting a case of delayed bleeding related to pancreatico-jejunosomy. This report illustrates the constantly expanding spectrum of applications for DBE both in the diagnosis and treatment of patients with altered bowel anatomy following complex surgical procedures.

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#### An Interesting Cecal Mass in a Patient with AIDS

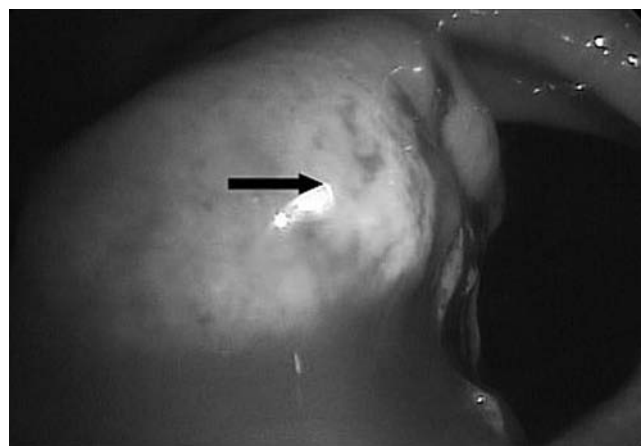
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**Purpose:** Disseminated histoplasmosis is a common opportunistic infection in AIDS patients who are severely immunocompromised. Gastrointestinal histoplasmosis (GIH) generally occurs in association with disseminated histoplasmosis or rarely as localized lesions. GIH is defined by radiological or endoscopic findings in conjunction with positive gastrointestinal tissue cultures or histopathologic observation of broad budding yeasts of *H. capsulatum* in tissue specimens. GIH typically occurs with median CD4 counts of 35 and patients naïve to anti-retroviral therapy. Common clinical features include fever, abdominal pain and diarrhea. Colon is the most frequently affected site (67%) followed by the cecum (17%). Endoscopic findings of GIH are usually multiple ulcers or pseudopolyps; however it can rarely present as a mass or constricting lesion suspicious for malignancy.

We describe a case of a 45-year-old white male with history of hemophilia A and AIDS. Patient was admitted to us with a three week history of sharp right lower quadrant abdominal pain and weight loss. Patient had no history of opportunistic infection and was naïve to anti-retroviral therapy. On physical examination, the right lower quadrant was tender to palpation with volun-



tary guarding. Laboratory examination revealed a CD4 count of 17/ $\mu$ L. A computed tomography (CT) scan of his abdomen showed a non-obstructing cecal mass with an 'apple-core' appearance highly suspicious for malignancy (marked by white arrow in Fig. 1). Subsequent colonoscopy showed multiple small ulcers in the cecum, ascending colon and the transverse colon with a three centimeter mass in the cecum (Fig. 2). Histopathology of the ulcers and the mass showed numerous intracellular budding yeasts consistent with *H. capsulatum*. Patient was started on itraconazole and reported resolution of abdominal pain during an outpatient follow-up after a three week period.[figure1][figure2]



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#### Diagnosis of Appendiceal Adenocarcinoma during Screening Colonoscopy

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**Purpose:** Screening colonoscopy allows visualization of the colon and appendiceal orifice. Careful inspection of the appendiceal orifice can lead to identification of appendiceal pathology.

**Presentation:** A 60-year-old man underwent colonoscopy for colon cancer screening. On inspection, the cecum appeared normal, however when air was aspirated prior to terminal ileum intubation, the tip of a pedunculated lesion prolapsed into the cecum from within the appendiceal orifice. Using a closed snare, a 15 mm polyp was everted from the orifice and removed by snare cautery.

**Clinical course:** The post-procedure course was notable for fever and abdominal pain that developed 12 hours after the procedure. An abdominal CT scan showed stranding around the cecal base, consistent with injury from the procedure. Symptoms resolved with oral antibiotics. The pathology revealed a villous adenoma with high-grade dysplasia. The cauterized margins were positive for adenomatous epithelium. The CEA level was normal. An abdominal MRI showed a normal appendix. He underwent repeat colonoscopy which showed a persistent polyp within the appendiceal orifice. This was biopsied and the pathology showed villous adenoma. The patient then underwent an appendectomy with removal of 1.0 cm of the cecum.

**Results:** Surgical pathology showed a moderately differentiated 0.3 cm mucinous adenocarcinoma present at the appendiceal ostium arising in a villous adenoma that encompassed the entire appendix and extended into the cecum. The margins were negative for adenoma or adenocarcinoma.

**Discussion:** Villous adenoma of the appendix is rare, with a frequency of 0.02% in appendectomy specimens. Adenocarcinoma of the appendix has been known to arise from within these adenomatous lesions, however there are only four case reports of appendiceal adenocarcinomas being diagnosed preoperatively by endoscopy. Early-stage appendiceal adenocarcinomas can

be cured by appendectomy or appendectomy plus cecectomy, however symptomatic patients are more likely to have unresectable disease. Other neoplastic lesions of the appendix reported to be visualized during colonoscopy include mucocoeles, mucinous cystadenomas and carcinoid tumors. Caution should be exercised with attempts at mucosal resection; a few case reports describe appendiceal intussusception or invagination that may appear polyp-like, and endoscopic removal may lead to complications.

**Conclusion:** Endoscopists should inspect the appendiceal orifice during colonoscopy and consider an appendiceal tumor when a polyp or deformity is seen.

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**Primary Pancreatic Non-Hodgkin's Lymphoma**

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**Purpose:** Primary pancreatic lymphoma is an extremely rare tumor. We present an unusual case of a primary large B cell diffuse non-Hodgkin lymphoma of the pancreas.

**Case Report:** This is a 72 year old Caucasian woman with past medical history of hypertension, depression and GERD who presented with worsening heartburn despite optimum therapy. Her examination and laboratory tests were unremarkable. The patient had a CT abdomen which suggested a pancreatic mass (4.5 × 2.5 cm), markedly distended gallbladder and multiple gallbladder stones. ERCP was unsuccessful. She underwent a CT guided pancreatic mass biopsy and a subsequent EUS guided biopsy. There were no malignant cells seen. She remained relatively asymptomatic for several months and refused either a more extensive work-up or a tertiary care center referral. A year later, she agreed for a second opinion and had an unsuccessful ERCP but now EUS revealed an infiltrative mass involving the head of the pancreas, the ampulla and the peri-ampullary area with surrounding lymphadenopathy. This time pathology reported a diffuse non-Hodgkin's Lymphoma of B cell origin. Immunostains were positive for CD45 and CD20 and negative for CD2 and chromogranin. After the diagnosis, she also developed supraclavicular lymphadenopathy. Patient was treated with chemotherapy (CHOP and rituximab), and did well. Patient is disease free two years after diagnosis and treatment.

**Discussion:** Extra nodal lymphoma of pancreas is extremely rare. Diffuse large-cell lymphoma is the most frequently observed pathological type. It is usually located in the head of the pancreas. Exact diagnosis is based on the histology and the immunohistology of the specimen. Our patient presentation was not typical. Except for an initial mild weight loss and upper gastrointestinal symptoms, she remained asymptomatic for the most part. Our initial suspicion was for a neoplastic process but with negative pathologic findings, it was thought that she may have an alternative diagnosis of chronic pancreatitis. Regardless, she was followed closely and on repeat evaluation, the correct diagnosis was made. Our patient was diagnosed more than a year since the initial symptoms.

**Conclusion:** In summary, this is a case report of a patient with a primary pancreatic lymphoma with atypical presentation and minimal symptoms. This case emphasizes the difficulty in making the diagnosis of pancreatic lymphoma and the need for persistent follow-up in patients with unexplained findings.

## 492

**Esophageal Lymphangioma**

Stephanie L. Hansel, MD, MS, Cuong C. Nguyen, MD\*. Gastroenterology, Mayo Clinic Arizona, Scottsdale, AZ.

**Purpose:** Lymphangioma is a soft tissue tumor that may appear in any organ except the brain. It most commonly involves the skin but has been found in various areas within the gastrointestinal tract. We present a very rare case of lymphangioma of the esophagus.

**Case Report:** A 68-year-old female with a 50-year history of Crohn disease predominately of the small bowel presented with dysphagia to solid food. Initial upper endoscopy revealed a 1-cm submucosal nodule at approximately 20-cm from the incisors (Fig. 1). Endoscopic ultrasound revealed a submucosal lesion with normal overlying mucosa at 21-cm from the incisor. The lesion was limited to the mucosal layers, measured 2.7 × 6.9 mm and was hypoechoic. Lesion was deemed resectable by the endoscopists and patient later underwent repeat upper endoscopy with jumbo forceps biopsy followed by total snare polypectomy without complications.

Pathology from the biopsy and polypectomy revealed the submucosa and lamina propria were occupied by a thin-walled lesion composed of anastomosing vessels containing proteinaceous fluid and occasional collections of lymphocytes. Adjacent tissue in the deeper portions of the biopsy showed a few benign lymphoid aggregates. No malignancy was seen. The findings were consistent with lymphangioma.

**Discussion:** Esophageal lymphangiomas are very rare. This is only the thirteenth reported case in the literature. Lymphangiomas consist of dilated lymphatic vessels and possibly form because of a failure to communicate with the lymphatic system. Mucosal biopsies may be misleading as these are submucosal lesions and therefore resection (endoscopic or surgical) is necessary for the definitive diagnosis. It is important to differentiate these tumors from other esophageal tumors that have the capability of undergoing malignant transformation. To date, there have not been any published reports of recurrence of esophageal lymphangioma tumors or malignant transformation.[figure1]



## 493

**Hemoclip for Severe Post-Prostate Biopsy Rectal Hemorrhage: Case Series**

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**Purpose:** Minor hematochezia is not uncommon after transrectal prostate biopsies. However, massive hemorrhage is rare, occurring in less than 1% of patients in large series. We describe four cases of post-prostate biopsy rectal hemorrhage in which hemoclip was used as part of combined modality endoscopic hemostasis.

**Methods:** Patients with significant gastrointestinal hemorrhage immediately following transrectal prostate biopsy were stabilized and volume



resuscitated. Flexible sigmoidoscopy was performed immediately after hemodynamic stabilization. All patients were treated with combined modality endoscopic therapy. Initially, epinephrine 1:10,000 was injected directly into and around the bleeding site. This was followed by placement of three hemoclips at the bleeding site. Once successful hemostasis was achieved, patients were monitored for rebleeding.

**Results:** Four patients developed rectal hemorrhage immediately following transrectal prostate biopsy. Three of the cases required hospitalization because of severe hemorrhage. One patient was managed in the emergency room and discharged the same day. Two patients developed shock, requiring emergent volume resuscitation. Three patients required transfusions for a mean of 5.7 units of blood [range 3 – 9 units]. The endoscopic stigmata were arterial spurting at the biopsy site in two patients, venous oozing and laceration at the apex of a large internal hemorrhoid in one patient, and non-spurting oozing in one patient. Successful hemostasis was achieved with endoscopic therapy. Rebleeding did not occur.

**Conclusion:** We describe four cases of post-prostate biopsy rectal hemorrhage controlled by combined modality endoscopic therapy. Patients with post-prostate biopsy hemorrhage, including severe hemorrhage can be successfully treated with epinephrine injection followed by hemoclip.

Post-Prostate Biopsy Rectal Hemorrhage

Case Number	Hospitalized	Units Transfused	Bleeding Stigmata
1	Yes	5	Arterial Spurter
2	Yes	3	Arterial Spurter
3	Yes	9	Venous Ooze/Hemorrhoidal Laceration
4	No	0	Slow Ooze

Clinical characteristics of patients with post-prostate biopsy rectal hemorrhage.

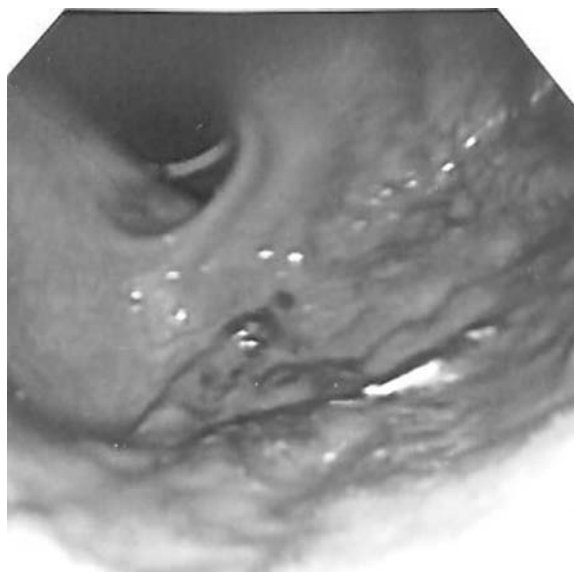
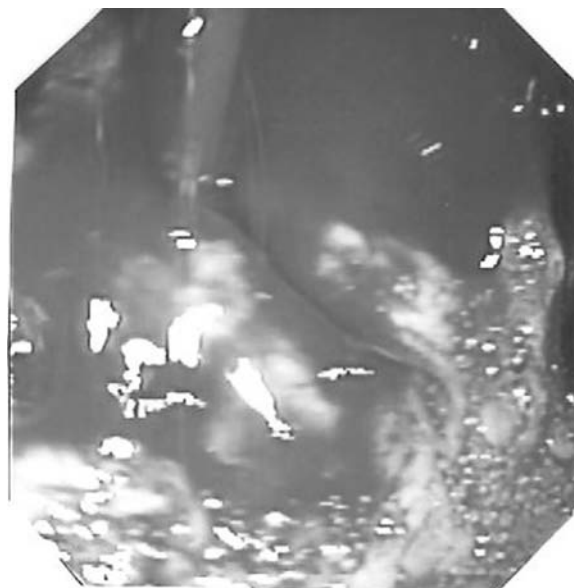
#### 494

##### Isolated Gastric Varices in Lymphoma

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**Purpose:** A 48 year old man with bipolar disorder was recently treated with clozapine. He was admitted to the hospital with pancytopenia and an episode of coffee ground emesis. Upper endoscopy showed patchy erythematous folds in the gastric fundus without evidence of bleeding. He received blood transfusions and was treated with a proton pump inhibitor. Clozapine was discontinued and hematology evaluation was in progress. A month later, he developed massive hematemesis, melena, and hypotension. Emergency upper endoscopy revealed actively bleeding vascular lesion in the gastric fundus (Fig. 1). Bleeding was controlled with hemoclips application, intravenous proton pump inhibitor, and Sandostatin. Repeat upper endoscopy the next day clearly demonstrated isolated varices in the gastric fundus (Figure 2). Computerized tomography of the abdomen showed a large splenic mass invading the capsule medially and encasing hilar vasculature. The next day, the patient underwent splenectomy with distal pancreatectomy. Pathology showed Large B-cell lymphoma involving the spleen and the pancreas with extracapsular and peripancreatic extension. Patient is receiving chemotherapy consisting of rituximab, cyclophosphamide, vincristine, prednisone, and doxorubicin.

**Conclusion:** This case illustrates the dramatic and rapid development of isolated gastric varices in conditions that induce splenic vein thrombosis. These conditions include chronic pancreatitis, acute pancreatitis, pancreatic carcinoma, hypercoagulable states, trauma, and lymphoma as seen in this patient. Splenectomy is necessary to control the ensuing life threatening upper gastrointestinal bleeding in addition to specific therapy to the underlying disease.[figure1][figure2]



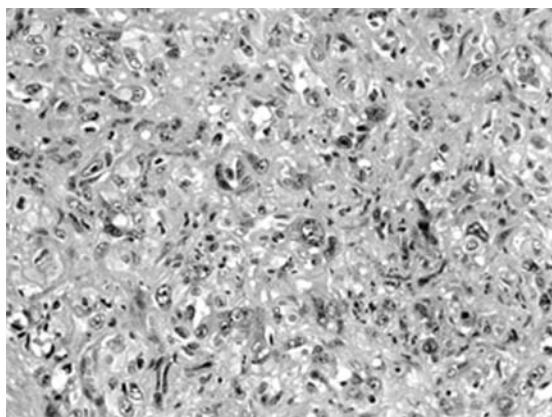
#### 495

##### Combined Hepatocellular Cholangiocarcinoma

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**Purpose:** A 60 year-old man presented with abdominal pain in early 2006. He had a history of cirrhosis due to HCV treated with pegylated interferon and ribavirin with a SVR in 2000. A liver biopsy in 2005 showed interval improvement with Grade 0 inflammation and stage 3 (bridging) fibrosis. Labs revealed a WBC count of 13,200 cells/mm<sup>3</sup>, platelet count of 202,000 cells/mm<sup>3</sup>, INR of 1.0, albumin of 4.4 g/dL, bilirubin of 0.5 mg/dL, AST of 33 U/L, ALT level 47 U/L, and alkaline phosphatase of 104 U/L. The alpha-feto protein level was 3 ng/ml (normal range 0–15 ng/ml). CT imaging revealed a 5 cm heterogeneous solid mass in the posterior segment of the right hepatic lobe (Figure A). Examination of the resected tumor revealed combined hepatocellular and cholangiocarcinoma (cHC-CC) with sarcomatous features (Figure B). Four months later the patient developed evidence of metastases to his humerus and cervical spine complicated by a humeral fracture. cHC-CC accounts for 1–6% of all primary liver cancers.<sup>1,2</sup>

Tumor heterogeneity and presence of cells intermediate between hepatocellular (HCC) and cholangiocarcinoma (CC) make it difficult to make an exact histologic diagnosis and predict the biologic behavior of the tumor.<sup>2</sup> cHC-CC is more aggressive than HCC with a natural course of invasion into the vascular system and metastasis to the lung and lymph nodes, carrying a poorer prognosis than ordinary HCC.<sup>2</sup> Survival of patients after hepatic resection is poorer than that of those with HCC. Components of cHC-CC that can be used to predict survival are the quantitative percent of tumor that is CC as well as the presence of sarcomatous features.<sup>2</sup> It is not known if adjuvant chemotherapy or liver transplantation are preferable options in the treatment of this unusual tumor. This patient was initiated on sorafenib, a novel therapy experimentally used for HCC.[figure1][figure2]



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#### Spontaneous Large Intramural Hematoma in Roux Limb of Gastric Bypass

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**Purpose:** Abdominal pain with a significant hematocrit drop may indicate severe GI bleeding. However, if there is no hematemesis, melena or hematochezia, bleeding from other sources must be considered. We describe a previously unreported case of spontaneous intramural bleeding within the Roux limb in a patient with a history of gastric bypass surgery.

**Methods:** A 34 year old woman, 13 days post bone marrow transplant for acute myeloid leukemia, with a history of Roux-en-Y gastric bypass surgery

2 years prior, developed moderate abdominal pain with Hct 28%, WBC 0.03 K/ $\mu$ L and platelets 6 K/ $\mu$ L. Esomeprazole and sucralfate were initiated, which did not relieve the pain. Over the next 3 days, the Hct dropped from 28% to 15%. The patient had more abdominal pain, tachycardia and hypotension. She had nausea, but no vomiting or hematemesis. She had regular bowel movements, no melena or hematochezia. After resuscitation with fluid, blood and platelet transfusions, the patient underwent an abdominal CT scan.

**Results:** On CT scan, there was an extensive intramural hematoma confined within the Roux limb of the gastric bypass with a wall thickness measuring up to 1.7 cm. The abnormality extended from the gastrojejunostomy to within a few centimeters of the jejunojejunostomy. The patient was given blood and platelet transfusions to maintain the Hct at 30% and platelet at 50 K/ $\mu$ L. The bleeding gradually stopped over a week. The patient's symptoms of abdominal pain and nausea resolved. A repeat CT scan one month later demonstrated complete resolution of the intramural hematoma from the Roux limb.

**Conclusion:** Spontaneous intramural small bowel wall hematoma has been reported in patients with excessive anticoagulation or with other risk factors for bleeding. The jejunum is the most common site of the hematoma, followed by the ileum and duodenum. Abdominal CT scan is the diagnostic modality of choice to detect an intramural hematoma. CT scan findings include circumferential or asymmetric wall thickening, intramural hyper-density, luminal narrowing, and intestinal obstruction. Accurate diagnosis is crucial because most patients can be treated nonoperatively with a good outcome. Resolution of the hematoma can be seen as early as 1 week after onset. In our case, the risk factor for bleeding was the extremely low platelet count. The patient responded well to conservative management. This is the first reported case of spontaneous intramural bleeding in the entire Roux limb of a gastric bypass.

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#### Successful Multi-Modality Endoscopic Treatment of Bouveret's Syndrome without Surgery

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**Purpose:** An 85-year-old man with dementia and diabetes presented with lethargy, nausea, and coffee-ground emesis. Vital signs were stable and laboratory examination was notable for a leukocytosis, hematocrit of 33%, and normal liver tests. CT scan showed a distended stomach, pneumobilia, and a 3 cm gallstone in close proximity to the duodenum. Endoscopy demonstrated a large gallstone impacted in the duodenal bulb, resulting in gastric outlet obstruction. Given the patient's age and comorbidities, the patient's surgeon requested endoscopic management. During the course of three endoscopies, the stone was fragmented using a combination of a Holmium:YAG laser and an intracorporeal electrohydraulic lithotripter (IEHL). IEHL was more effective in uniformly shattering the stone's softer outer shell, while the laser was more effective in weakening the stone's internal structure by boring holes into its harder, inner core. The largest fragment was extracted using a double-snare technique, which provided extra grip and leverage. A large cholecystoduodenal fistula was visualized with surrounding ulcerated mucosa, and the gastroscope could be easily advanced into the gallbladder lumen. The patient was discharged to a nursing home, without recurrence of symptoms.

**Discussion.** Gastric outlet obstruction by a gallstone migrating through a cholecystoduodenal fistula (Bouveret's Syndrome) was first described in 1896 and is a rare condition, representing fewer than 5% of cases of gallstone ileus. Patients are often elderly with underlying comorbidities which poses significant challenges to both surgeon and endoscopist. Despite modern surgical techniques, mortality is as high as 30%. Since 1985 there are only a few reports of successful management with endoscopy alone, with more than 90% ultimately requiring surgery. Our experience suggests that

endoscopists should initiate stone fragmentation with IEHL as first line management, use laser lithotripsy adjunctively, crush stone fragments that are left in the stomach to prevent migration and ileal obstruction, and prepare for multiple endoscopic sessions. The choledochoduodenal fistula does not require closure. With an aging, obese population, we anticipate Bouveret's to become more common and recommend endoscopists become familiar with the multiple options available for effective endoscopic therapy.

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### An Unusual Case of Headache in a Patient with Ulcerative Colitis

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**Purpose:** Cerebral vessel/sinus thromboembolism is a rare complication of IBD, with DVT and PE accounting for the majority of thromboembolic complications in patients with IBD. Afflicted patients are usually young and without other risk factors for thrombosis other than IBD.

**Case report:** A 21-year-old male with chronic ulcerative colitis (UC) was admitted with exacerbation of colitis despite therapy with corticosteroids, oral mesalamine and 6-mercaptopurine (6-MP). Flexible sigmoidoscopy and biopsies were consistent with severe colitis and negative for infectious etiologies. A CT of the abdomen demonstrated pancolitis. Laboratory values were notable for an elevated ESR and thrombocytosis. After initiation of IV steroids, the patient's colitis improved, but one week after admission, he developed a new bilateral unremitting headache. Over the next 24–48 hours, the patient complained of nausea, vomiting, and dizziness with standing. The neurological exam was significant for increased somnolence, horizontal nystagmus, right-sided facial weakness, dysmetria, and right upper extremity drift. MRI/MRV of the head showed venous infarction involving the cerebellum secondary to venous thrombosis of the bilateral transverse sinuses, straight sinus, and bilateral internal cerebral veins. The patient was started on unfractionated heparin. An attempt at recannulization of the right cerebral sinus was unsuccessful. Infectious etiologies were excluded, and additional testing for hereditary hypercoagulable states was negative. The patient's mental status gradually improved, with complete resolution of neurologic and GI symptoms. He was discharged on mesalamine, oral steroids, and 6-MP with plans for a six month course of oral anticoagulation with coumadin.

**Discussion:** Cerebral sinus and venous thromboses are rare complications of IBD, with a reported frequency of ~ 0.1%. It has been suggested that this complication is more frequent in UC compared with Crohn's disease. MRI/MRV is the most sensitive non-invasive diagnostic imaging technique, but if the diagnosis is still uncertain, angiography should be considered. Anticoagulation with heparin followed by coumadin is a safe, effective therapy. In a prospective study, 80% patients with cerebral sinus/vein thrombosis treated with heparin made a complete recovery (ISCVT study). Optimal duration of treatment is unknown, but usually given for six months after a first episode. To our knowledge, thrombolysis has been limited to case reports and uncontrolled studies.

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### Primary Sclerosing Cholangitis in Association with Multiple Myeloma

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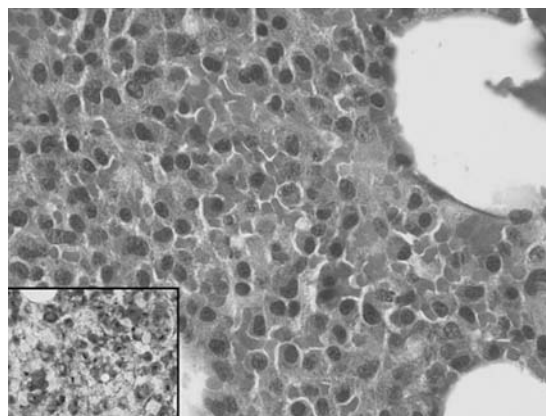
**Purpose:** We report the second known case of multiple myeloma (MM) associated with primary sclerosing cholangitis (PSC).

#### Methods: CASE REPORT

**Results:** A 57-year-old man presented with a 6 month history of jaundice with total bilirubin of 6.3 mg/dL, associated with increased alkaline phosphatase to 800 unit/L. Workup included ERCP (Fig. 1) which confirmed PSC

and biopsy confirming cirrhosis. In the course of his pre-transplant evaluation, he developed marked malnutrition with a decrease in serum albumin from 3.6 to 2.0 g/dL and hypercalcemia. Lytic lesions were identified in the humerus on routine X-rays. A monoclonal IgG -kappa restricted serum immunofixation and significant kappa light chains in the urine (1790 mg/L) were found. Figure 2 is a high power photomicrograph of H & E stained marrow clot section from a biopsy of the humeral lesion, showing marrow replacement by plasma cells- some with binucleation. The inset shows strong staining for kappa light chains, confirming that lesion is monoclonal for kappa light chains- consistent with monoclonal plasma cell dyscrasia (PCD). Given the confirmation of multiple myeloma and advanced cirrhosis, palliative care was initiated.

**Conclusion:** This case is the second report to suggest the possible association of MM with PSC. PCD encompasses a number of disorders with MM being the most serious. PCD is often associated with other chronic liver diseases such as chronic active hepatitis, autoimmune hepatitis, and primary biliary cirrhosis. It is thought that chronic antigenic stimulation by the cirrhotic liver selects B cell clones which may eventually become malignant. This case highlights the possible connection between MM and PSC.[figure1][figure2]



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### Concomitant Hemobilia and Hepatic Abscess after Radiofrequency Ablation

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**Purpose:** A 79 year-old male with coronary artery disease, hemophilia A, hepatitis C cirrhosis and hepatocellular carcinoma (HCC) presented ten days

status post radiofrequency ablation (RFA) with two days of recurrent hematemesis, melena, right upper quadrant pain and fever. The patient's HCC was previously deemed unresectable due to his comorbid conditions, and the proximity of the 3.5 cm hepatoma to the bile ducts and the portal vein. On exam, he was pallid with profuse hematemesis and tachycardia. His WBC count was  $27.1 \times 10^3/\text{mL}$  (3.6–11.1) and hematocrit was 30.2% down from 39.9% two days prior. His factor 8 level and platelets were normal, with an INR 1.29, PTT of 55.2s (25.0–39.0) and minimally elevated liver function tests. EGD showed blood spewing from the ampulla signifying hemobilia. Emergent angiography did not show active bleeding, but empiric embolization was performed to an irregular branch arising from the left hepatic artery, which coursed along the needle tract from the recent RFA therapy. A CT scan showed an  $8.4 \times 4.8$  cm heterogeneous area containing debris, hemorrhage and air in the medial segment of the left hepatic lobe of the liver, consistent with an early post-RFA abscess. The patient responded to antibiotics and volume resuscitation, and was later discharged home. He has subsequently tolerated a second RFA ablation.

**Discussion:** RFA is a safe and effective therapeutic option for unresectable HCC with five year survival rates comparable to surgical resection. Complications occasionally arise from mechanical and thermal injury to vascular structures, the biliary tree and adjacent organs. Examples include portal and hepatic vein thromboses, subcapsular hematomas, and bile duct stenoses. Hemobilia is a rare complication of RFA with a prevalence of 0.3%. Most reported cases have favorable prognoses and do not require intervention. In our case, mechanical injury to the hepatic vasculature during RFA catheter placement was thought to be the etiology of the patient's hemobilia, although thermal damage may have also contributed. In addition, our patient presented with concurrent symptoms and radiological findings consistent with an early abscess in the post-RFA hepatic tissue. Thus, inflammatory damage from the concomitant infection may have contributed to the hemobilia. Our case illustrates the importance of early recognition and treatment of the rare complications of RFA therapy including hemobilia and hepatic abscess.

## 501

### Spontaneous Multiperforation in Lymphomatous Colitis Masquerading as Crohn's Disease: Two Cases

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**Purpose:** Lymphomatous colitis is a rare disorder that can simulate inflammatory bowel disease. We describe 2 cases of lymphomatous colitis mimicking Crohn's disease that were complicated by spontaneous multiperforation. **Case 1:** An 82 year old female with a history of chronic lymphocytic leukemia presented with progressive diarrhea over 5 months, associated with a 20 pound weight loss. Colonoscopy showed moderately severe pancolitis with ileal inflammation. Biopsies were reported as inflammatory colitis. She failed to respond to high dose corticosteroids. Within 4 weeks she required emergent colectomy for spontaneous multiperforation of her colon. Pathology revealed colonic and ileal MALT lymphoma. The colonic lymphoma was distinct from her chronic lymphocytic leukemia, since the former was negative to CD5 and did not have chromosomal trisomy 12, whereas the latter was CD5 positive and positive for trisomy 12. This indicates that the patient had 2 distinct lymphoproliferative diseases. In retrospect, immunoperoxidase stains on the initial biopsies did reveal malignant monoclonal lymphocytes. (See Table)

**Case 2:** A 49 year old female with a history of ulcerative colitis presented with severe watery diarrhea and a 50 pound weight loss. Colonoscopy revealed severe pancolitis with skip areas of normal colon. Biopsies were reported as inflammatory colitis. She failed to respond to high dose corticosteroids, and refused surgery. Within a number of weeks, she required emergent colectomy for spontaneous multiperforation of her colon. Pathology revealed primary colonic non-hodgkins lymphoma (NHL). In retrospect,

immunoperoxidase stains on the initial biopsies did reveal malignant monoclonal lymphocytes. (See Table)

**Conclusion:** Lymphomatous colitis can mimic Crohn's colitis. Lymphomatous colitis should be considered in patients with steroid-refractory inflammatory bowel disease. Earlier diagnosis with immunoperoxidase stains looking for monoclonal proliferation of malignant lymphocytes, may prevent progression of necrotizing lymphoma and spontaneous multiperforation.

Lymphomatous Colitis: 2 cases

	Case 1	Case 2
Primary Colonic Lymphoma	Disseminated	Primary
Prior IBD	No	Yes
Mimicking	Crohn's	Crohn's
Steroid refractory	Yes	Yes
Perforation	Yes $\times$ 3	Yes $\times$ 3
Classification of Lymphoma	MALT	NHL

Characteristics of the two cases of lymphomatous colitis.

## 502

### Efficacy Alendronate for Improving Bone Mineral Density in Celiac Disease

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**Purpose:** Currently there is no study or report regarding using bisphosphonate in young males with osteoporosis caused by celiac disease.

**Case Report:** A 32 year old South Asian man initially presented to a gastroenterologist after abnormal liver function tests and mild anemia were detected on a routine office visit. Physical examination was normal. Initial aminotransferases tests showed aspartate aminotransferase (AST) of 31 U/L and alanine aminotransferase (ALT) of 56 U/L. Biopsy of the second part of the duodenum showed villous atrophy with crypt elongation, replacement of surface epithelial cells by cuboidal cells with loss of brush border and increase in lymphocytes relative to the number of epithelial cells. Lamina propria showed increased plasma cells, lymphocytes and polymorphs consistent with celiac disease. Bone scan revealed osteoporosis involving lumbar spine and osteopenia involving both hips. T and age matched Z scores for lumbar spine were  $-2.8$  and  $-2.4$ ; right hip were  $-1.9$  and  $-1.7$ ; and left hip were  $-2.1$  and  $-1.9$ . Patient was started on a strict gluten free diet and alendronate 10 mg per oral daily. Repeat biopsies of the duodenum showed regeneration of villous height and regression of crypt hyperplasia and the surface epithelium showed increased columnar cells with basal nuclei and brush borders consistent with partial restoration and improvement in celiac disease. Repeat bone scan 18 months later showed osteopenia with significant improvement of bone mineral density. Post therapy T and age matched Z scores for lumbar spine were  $-1.9$  and  $-1.6$ ; right hip were  $-2.0$  and  $-1.7$ ; and left hip were  $-1.7$  and  $-1.4$ . No significant symptoms related to side effects of alendronate were reported during the 18 months treatment period. Repeat aminotransferases tests revealed AST of 26 U/L and ALT of 42 U/L.

**Conclusion:** The significant increase of BMD in our patient after receiving alendronate is the first case report of alendronate treatment in celiac disease. Previous studies of alendronate therapy among men with secondary osteoporosis included only patients with long term corticosteroid treatment, low serum testosterone, and malabsorption syndrome without specific diagnosis of celiac disease. Study comparing gluten free diet therapy and gluten free diet therapy with bisphosphonate, especially in non-postmenopausal women, may reveal the efficacy of bisphosphonate in celiac disease.

## 503

### Unusual Cause of Chronic Diarrhea: Cronkhite-Canada Syndrome

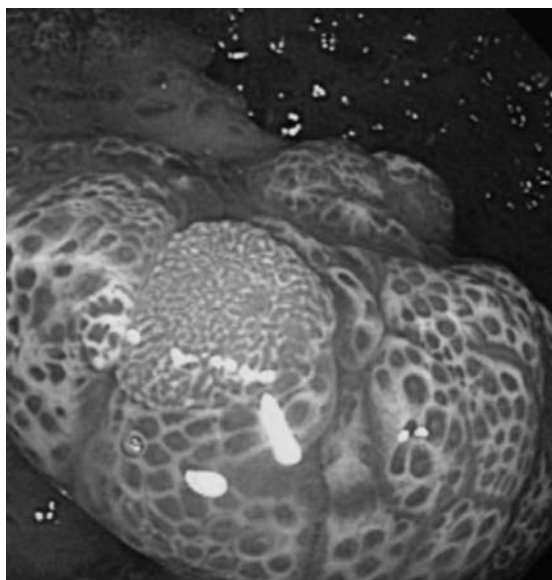
Manmeet Padma, MD, Jenica Ryu, MD, Nahid Molaie, MD, Eric Olsen, MD, Viktor Eysselein, MD, David Chung, MD, Binh V. Pham, MD\*.

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**Purpose:** Cronkhite-Canada syndrome (CCS) is one of the rare non-familial causes of multiple polyposis characterized by diffuse gastrointestinal polyposis, alopecia, onchodystrophy, and hyperpigmentation. Herein, we describe a case of CCS who presented with chronic diarrhea and weight loss.

**Case Report:** A 37 year old Filipino man with no PMH presented with a 5 month h/o post-prandial emesis, diarrhea, occasional hematochezia, and weight loss of 45 lbs. He reported no fevers or other affected family members. One week after the onset of his symptoms he noted darkening of palms and soles, loss of scalp and facial hair, and softening of nails. The patient appeared pale and cachectic. There were small hyperpigmented macules on the palate, palms, and soles, hyperpigmentation of hands, feet and back, dystrophy of the nails, alopecia of scalp and eyebrow, and pitting edema of lower extremities. His abdomen had diffuse tenderness. Laboratory data revealed leukocytosis, hypoalbuminemia, deficiency of vitamin A and D. EGD revealed diffuse polypoid lesions starting from the cardia to the 3rd portion of the duodenum. Similar lesions carpeted the entire colon (Fig. 1). SBFT revealed only involvement of the duodenum. Histology revealed polypoid inflammatory mucosa with cystic dilatation of foveolae in the stomach and of colon mucosal glands, confirming the diagnosis. The nutritional support was given with TPN. The patient was started on oral prednisone, histamine blocker, proton pump inhibitor, metronidazole, and subcutaneous octreotide. Vitamins and minerals were supplemented. His condition gradually improved and was sent home on TPN. Follow-up after one month revealed toleration to oral feeds, normalization of bowel habit, improvement of alopecia and onchodystrophy.

**Discussion:** CCS is the rare cause of non-familial multiple polyposis. The diagnosis is based on clinical, endoscopic and pathological findings. Eventually, most of the patients develop protein-losing enteropathy and malnutrition. The prognosis remains poor, with few patients surviving more than few months after the diagnosis and 5-year mortality up to 55%.[figure1]



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#### Metastatic Cholangiocarcinoma Presenting as Left Shoulder Pain

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**Purpose:** Cholangiocarcinoma carries a poor prognosis in part due to late diagnosis of the condition. Early diagnosis by recognizing the initial symptoms and risk factors is critical to a better outcome.

**Methods:** A 52 year-old woman with hepatitis C, tobacco use, and symptomatic cholelithiasis was admitted for elective cholecystectomy. She also complained of 2 months of severe left shoulder pain and denied any weight loss. Physical exam revealed RUQ tenderness and severe left scapular pain. Laboratory results were remarkable for alkaline phosphatase of 449 U/L, AST 86 U/L, and ALT 206 U/L. Left shoulder X-ray revealed a lytic lesion in the scapula. MRI showed a 4.5 × 3.8 × 5.0 cm mass in the left scapula. A CT guided needle aspiration biopsy revealed adenocarcinoma. Abdo CT showed multiple masses in the liver. An upper endoscopy, colonoscopy, and CT of the chest were normal. At exploratory laparotomy, a tumor encasing the perihilar area and portion of the liver was identified. Biopsy revealed cholangiocarcinoma. Patient opted for hospice care.

**Results:** Cholangiocarcinoma accounts for 10–15% of hepatobiliary neoplasms. This condition should be included in the differential diagnosis of chronic RUQ pain in patients with risk factors such as primary sclerosing cholangitis, choledochal cyst, chronic intraductal stones, and congenital anomalies of the bile ducts. However, recent findings have suggested additional risk factors like HCV, HIV, cirrhosis, diabetes and smoking. Our patient had 2 risk factors: HCV, and smoking history. Cholangiocarcinoma usually metastasizes to the lungs, adrenal glands, brain, lymphatic system, and the axial skeleton. Metastasis to appendicular skeleton is rare with 2 cases reported. Traditionally, ERCP is used to assist the diagnosis, but non-invasive techniques like magnetic resonance cholangiopancreatography (MRCP) are now preferred. A recent study comparing ERCP and MRCP found that both were equally effective in diagnosing biliary obstruction. Due to its late presentation, cholangiocarcinomas have an extremely poor prognosis, with an average five-year survival rate of 5–10%. Surgical resection is the only curative treatment and is possible in early extrahepatic cholangiocarcinoma. Otherwise, chemotherapy with gemcitabine and cisplatin provides a modest response. Biliary stents are useful for palliation of biliary obstruction.

**Conclusion:** Cholangiocarcinoma should be considered in patients with chronic RUQ pain who in addition have risk factors noted above.

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#### A Case of *Vibrio Vulnificus* Septicemia in a Patient with Alcoholic Liver Disease

*Mark J. Marino, MD\*, David Matherne, DO, Arthur E. Richert, MD. Gastroenterology, LSU Health Sciences Center, New Orleans, LA.*

**Purpose:** A 57 year old male commercial fisherman presented to Leonard J Chabert Medical Center in Houma, Louisiana in the early afternoon complaining of back pain, arm pain and shortness of breath after falling off a fishing pier into (brackish) water earlier that day and suffering lacerations to both of his forearms. He also stated that he swallowed a small amount of water. This patient had no known previous medical history but did not regularly visit a physician. Through his family it was obtained that he had an extensive history of alcohol consumption but had never been diagnosed with advanced liver disease.

Physical exam upon presentation was significant for normal vital signs, spider angiomas on chest wall, and erythematous areas on both forearms consistent with cellulitis. His labs were significant for AST 74, ALT 27, Total Bilirubin 3.3, and INR of 1.4 and a WBC count of 7300. His platelet count was 55,000. Cardiac enzymes were negative. He was placed on broad spectrum antibiotics including doxycycline. Within 6 hours blood cultures were positive for *Vibrio vulnificus*. In the first 12 hours after admit patient suffered cardiopulmonary arrest but was successfully resuscitated via ACLS protocol. At the time of this abstract submission, the patient is still alive but critically ill in the ICU approximately one month after admission. His hospital course has included multi-organ failure including ARDS, renal failure requiring dialysis, and ischemic hepatitis. He did not develop fulminant hepatic failure. He did develop ascites and encephalopathy which have been controlled. His wounds have been extensively debrided and he has undergone

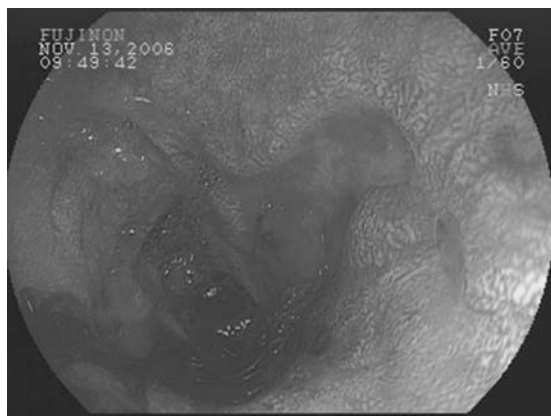
amputation of several of his digits. *Vibrio vulnificus* septicemia is a severe illness often associated in patients with advanced liver disease of any kind most often with alcoholic liver disease. Patients are infected through open wounds in estuarine water and consumption and handling of shellfish. The mortality in patients with advanced liver disease is greater than 50%. It must be considered in any patients with known or suspected liver disease, diabetes, or otherwise compromised immune systems.

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#### **MALT Lymphoma of the Duodenum: A Rare Cause for Upper Gastrointestinal Bleeding and Pancreatitis**

Michael Selden, MD\*, Patricia Sanchez, MD, Esmat Sadeddin, MD, Sandra Laya, MD, Wendell Clarkston, MD. Gastroenterology Department, Saint Luke's Hospital/University of Missouri, Kansas City, Kansas City, MO.

**Purpose:** Mucosa associated lymphoid tissue lymphoma of the duodenum represents a rare neoplasm. A review by Xiang et al[i] in 2004 highlighted only 17 previous cases of duodenal MALT lymphoma in the English literature. We report another rare case of duodenal MALT lymphoma. A 56 y.o. female presented with upper GI bleeding and acute pancreatitis. Upper endoscopy demonstrated an irregular ulceration in the second portion of the duodenum (Fig. 1). Endoscopic biopsies revealed acute and chronic inflammation. An abdominal CT scan demonstrated significant circumferential mural thickening involving the second portion of the duodenum and evidence of pancreatitis. Despite unremarkable endoscopic biopsies, the irregular appearance of the ulcer and CT findings raised suspicion of underlying malignancy. The surgical service performed an exploratory laparotomy. A nodular mass in the second portion of the duodenum extending into the pancreas was noted. Biopsy of the mass revealed a low grade MALT lymphoma. The patient recovered from her episode of pancreatitis and started radiation therapy. Patel et al.[ii] have previously reported a patient with duodenal MALT lymphoma with pancreatic infiltration. However, this is the first report of pancreatitis from the extension of a duodenal MALT lymphoma. This case hopes to expand the current knowledge of the possible presentations of this rare entity. [i] Xiang Z, Onoda N, Ohira M et al. Mucosa-associated lymphoid tissue lymphoma of the duodenum: a report of a case resistant to *Helicobacter pylori* eradication. *Hepatogastroenterology* 2004; 51(57): 732-5. [ii] Patel VG, Eltayeb OM, Henderson VJ et al. Primary duodenal low-grade mucosa-associated lymphoid tissue lymphoma presenting with outlet obstruction. *American Surgery*. 2004; 70(7): 613-6.[figure1]



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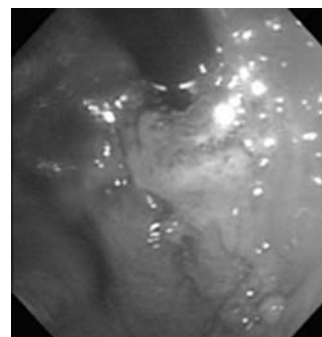
#### **Gastric Adenocarcinoma in MEN-1**

Jessica L. Widmer, DO, Jay P. Babich, MD, Bijou Abraham, DO, Phillip Cassar, MD, Kavita R. Kongara, MD, James H. Grendell, MD\*. Gastroenterology, Winthrop University Hospital, Mineola, NY.

**Purpose:** Multiple Endocrine Neoplasm Type 1 (MEN 1) is a familial syndrome in which tumors develop in the parathyroid, pancreatic, and pituitary gland. The frequency of MEN 1 is about 1/30,000. Gastrinomas are the most common, symptomatic pancreatic endocrine tumor in MEN I, with ZE Syndrome and esophageal strictures being known complications.<sup>1</sup> A 63-year-old male was admitted with a one month complaint of dysphagia to solids and liquids; as well as nausea, vomiting, and a 17 lb. weight loss. He has a known history of ZES with metastatic gastrinoma, parathyroidectomy, and a diagnosis of MEN-1. Prior to admission he had a gastrin level of 13,382 pg/mL and a CT of the abdomen that demonstrated ascites, soft tissue infiltration involving the omentum and the mesentery consistent with carcinomatosis. Admission exam revealed tenderness in the lower quadrants of the abdomen. Laboratory data were normal. EGD revealed an esophageal stricture that was subsequently dilated and a large nodular gastric mass that was contiguous with the g-e junction (Fig. 1). In addition to gastritis biopsies showed invasive poorly differentiated gastric adenocarcinoma with signet ring features and areas of gastric type epithelium with nodular proliferation of cells suggestive of neuroendocrine tumor. The patient tolerated his dilatation without complication and was discharged home.

There is no documented association between MEN 1 and gastric adenocarcinoma. Hoffman et al. hypothesized that patients with MEN-1 with gastrinomas have an increased risk of severe esophageal disease including strictures and Barrett's.<sup>1</sup> Their findings suggest that prolonged inadequately controlled acid secretion increases the risk of developing advanced esophageal disease and the possibility of esophageal adenocarcinoma. We hypothesize that when gastric mucosa is exposed to uncontrolled acid hypersecretion, caused by increased gastrin levels, gastric adenocarcinoma could develop.

**REFERENCE** 1. Hoffman, K, et al. Patients with MEN I with gastrinomas have an increased risk of severe esophageal disease including stricture and the premalignant condition, Barrett's Esophagus. *The Journal of Clin Endocrinology & Metabolism*. 2006; 91 (1): 204-212.[figure1]



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#### **Pyogenic Liver Abscess Secondary to Staphylococcus aureus Infection without Primary Source of Infection**

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**Purpose:** A 46 year old African-American male, migrated from Africa, presented with chief complaint of productive cough for 2 months associated with pleuritic chest pain, fever for 3 days, night sweats, mild shortness of breath and loss of appetite. The patient denied hemoptysis, weight loss, recent travel. Past medical history was significant only for GERD. He reported a history of Penicillin allergy. He is a smoker, but denied alcohol or drug use. His vital signs were Temp of 103 F, Pulse 130/min, Respiratory rate 28/min, Blood pressure of 140/75 mmHg and oxygen saturation was 98% on room air. Lab values were significant for WBC of 11.7, Hemoglobin/hematocrit of 14.4 gm/dl/41%, Platelet count of 319. Blood cultures done on admission were negative. Liver function tests were elevated and chemistry was normal. He was admitted with the impression of Pneumonia and started on

intravenous Levofloxacin. Official Chest x-ray report revealed no active pulmonary disease. Hepatitis B and C serology was negative except for reactive Anti-Hepatitis B core antibody. Repeat CBC showed a slight decrease in the WBC count but the LFTs remained elevated. Infectious Disease was consulted. HIV testing was negative. CT of chest with contrast showed a 7 cm mass in the right lobe of the liver. Triple phase Liver Scan was done which showed a 7–8 cm fluid filled abscess and a Gastroenterology evaluation was requested. Serology testing for *Echinococcus granulosus* and *E. histolytica* were negative. Radiological guided drainage of the liver abscess showed a purulent material with cell count as follows: WBC 285000, RBC 57500, Neutrophils 27%, Lymphs 65%. Culture grew methicillin resistant *Staphylococcus aureus*. The patient was treated with Vancomycin and the WBC and LFTs started to decrease. Whole body Gallium Scan was negative and Echocardiography didn't show any vegetations. The patient was discharged home on oral Clindamycin. The patient was seen in clinic for follow up and reported complete improvement in symptoms and repeat CT scan showed resolution of the Liver abscess. The most striking point in this case is there was no primary source of infection from *Staphylococcus aureus* found.[figure1]



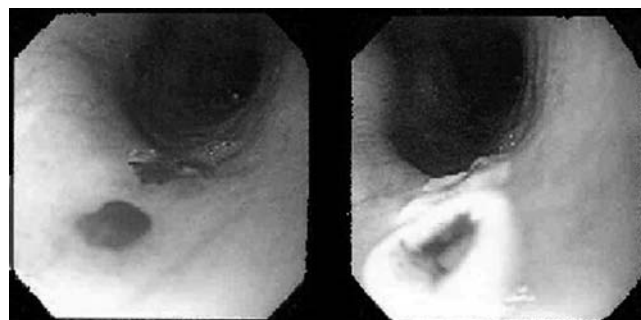
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#### Dieulafoy's Lesion of Esophagus Managed with Injection Therapy

Lokesh K. Jha, MD, Fredrick Fallick, MD\*. Department of Gastroenterology, St. Barnabas Hospital, Bronx, NY.

**Purpose:** We report the case of a 25-year-old male from Gambia, West Africa who presented complaining of vomiting bright red blood for 3 days. He had been seen in emergency department of a different hospital 3 days prior and sent home, as the vomiting had resolved. He subsequently had 1 episode hematemesis so he came to our ED for further evaluation. He reported passing black stool on one occasion. He denied abdominal pain, fever, dizziness, and shortness of breath. He denied smoking, alcohol use, or use of any drugs, except that he had taken a total of 4 Advil tablets prior to seeing melena. On examination, he was afebrile, slightly tachycardic with a pulse of 108; BP was 142/85 with no orthostasis. The abdominal exam revealed a soft, non-tender abdomen with normoactive bowel sounds. Stool guaiac was positive. Laboratory values were as follows: hemoglobin and hematocrit (H&H) 5.7 g/dl/16.3%; INR 1.3; BMP values were within normal limits. Chest x-ray and plain abdominal film revealed no significant findings. EKG demonstrated sinus tachycardia at 105 bpm, but was otherwise unremarkable. GI consultation was requested, and 4 units of PRBC transfusion were

recommended to keep hemoglobin above 9. Subsequently, the patient was taken for upper endoscopy. Upper endoscopy revealed an actively bleeding Dieulafoy's lesion in the mid esophagus, along with a hiatal hernia, which was controlled with sclerotherapy using epinephrine and cautery with BI-CAP. The patient was monitored in the ICU, the blood counts stabilized, and there were no further episodes of hematemesis or melena. The patient was subsequently discharged home on a proton pump inhibitor. Discharge H&H were 7.6 g/dl and 21%. Three days later, he returned to the ED complaining of constipation. On this admission, guaiac was positive and the H&H were 7.1 g/d and 21.0%. GI consultation was again requested, and the patient was taken for repeat upper endoscopy which demonstrated both cauterized lesions in the esophagus to be well-healed with a clean, white base and no evidence of recurrent bleeding. The H&H remained stable, and the patient was discharged home on iron tablets and followed in the GI clinic with no episodes of recurrent bleeding.[figure1]



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#### Diarrhea: A Presenting Symptom of HCC

Paul S. Panzarella, MD, Jay P. Babich, MD, Robert Bonasera, MD, Kavita R. Kongara, MD, James H. Grendell, MD\*. Gastroenterology, Winthrop University Hospital, Mineola, NY.

**Purpose:** Hepatocellular carcinoma (HCC) is a primary malignancy of the liver; most cases are secondary to hepatitis or cirrhosis. The presenting symptoms of HCC include abdominal pain, jaundice, and bone pain. We report a case of HCC diagnosed in a patient with a one-month complaint of watery diarrhea.

A 43-year-old female presented to our institution with one month of abdominal pain, nausea, vomiting and early satiety. Patient had been working as a missionary in Portugal 8 months prior to presentation; about 1 week after her arrival, she began to have watery diarrhea (5–6 episodes/day) for which she states she received "pills." CT abdomen and pelvis followed by a liver biopsy were performed while the patient was in Portugal. She was given a diagnosis of cancer after a mass was seen on CT and liver biopsy exhibited evidence of malignancy. The patient relocated to the USA. Upon arrival she described her pain as crampy, radiating to the right flank associated with nausea and bilious vomiting. She reported as well to have had an unintentional weight loss of 50 lbs in the last 8 months with loss of appetite.

Pertinent physical exam findings were a palpable liver 7 cm below the costal margin and diffusely across the entire abdomen.

Laboratory data is shown below in Table 1. A liver biopsy revealed proliferation of neoplastic cells resembling hepatocytes, arranged in large trabeculae and nests, giving the impression of a well-differentiated liver carcinoma.

The patient was admitted and based on the extent of the lesions, had bland particle embolization of the left lobe of the liver with improvement in her abdominal pain, and was subsequently able to be discharged tolerating oral feeds.

The literature citing diarrhea as a presenting symptom of HCC is scarce.

In the approach to the patient with a liver mass and diarrhea the clinician should consider HCC in addition to carcinoid and other neuroendocrine tumors.



## Laboratory Values

Total Bilirubin	2.0 mg/ul
Direct Bilirubin	1.5 mg/ul
AST	448 U/l
ALT	185 U/l
ALKP	185 U/l
GGTP	868 U/l
Tot Protein	7.6 g/dl
Albumin	3 g/dl
CEA	1 ng/ml
Hepatitis Profile	non-reactive
ANA	40
AMA	20
ASMA	20
Ferritin	103 ng/ml
Alpha-1-anti-trypsin	152

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**A Case of Multiple Gastrointestinal Stromal Tumors of the Small Bowel in a Patient with Neurofibromatosis Type 1**

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**Purpose:** Gastrointestinal stromal tumors are rare tumors of the gastrointestinal tract that arise from primary mesenchymal cells. However, in patients with type 1 neurofibromatosis (NF-1), GISTs have been reported to occur with increased tendency. NF-1 is a neurocutaneous disorder that involves neuroectodermal and mesenchymal derivatives, and it is associated with GISTs of the small bowel. Clinical behaviors of GIST include abdominal pain, intestinal obstruction, and acute or occult gastrointestinal bleeding. We herein report a case of a patient with NF-1 with acute gastrointestinal bleeding from multiple GISTs of the small bowel.

**Case Report:** A 57 year-old male with known NF-1 presented with melena and anemia. His past medical history was significant for gastric angiectasias. On presentation, he had evidence of neurofibromas on his face and upper extremities. He denied any abdominal pain. Laboratory analysis showed severe anemia with a hemoglobin of 9 g/dl. An upper endoscopy revealed a non-bleeding mass in the second to third portion of the duodenum. A subsequent colonoscopy and capsule endoscopy were unremarkable. Biopsy of the duodenal mass demonstrated a spindle-cell neoplasm with positive c-kit protein, suggestive of a GIST. Computed tomography revealed multiple masses as large as 3 × 4 cm in the small bowel. Exploratory laparotomy found multiple duodenal and jejunal tumors with biopsies that were consistent with GIST of low risk (<2/50 HPF mitotic index). The patient received a prepyloric-preserving Whipple resection. The rest of his hospital course was uneventful. His H/H stabilized, and he was discharged.

**Conclusion:** GISTs of the small bowel are very rare and may present with massive bleeding. Particularly in patients with type 1 neurofibromatosis with gastrointestinal bleeding, it should be considered as part of the differential.

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**Domperidone for the Treatment of Severe Hyperemesis Gravidarum**

Sumona Saha, MD, Rosanna Moura, MD\*. *Division of Women's Digestive Disorders, Women & Infants' Hospital, Providence, RI.*

**Purpose:** Hyperemesis gravidarum (HG) is a condition of severe nausea and vomiting during pregnancy leading to dehydration, nutritional deficiency, and increased fetal morbidity and mortality. We describe a case of a pregnant woman with twin gestation and intractable HG leading to desire to terminate the pregnancy who was successfully treated with domperidone.

**Case:** A 33 year-old female, gravida 2, para 1 with twin gestation presented with severe HG. Intractable nausea and vomiting began at 5 weeks gestation. Work-up for other causes of nausea and vomiting in pregnancy was negative. Treatment with standard oral therapy, IV hydration and IV ondansetron was ineffective. IV metoclopramide was helpful; however, the patient developed jaw clenching leading to its discontinuation. At 12 weeks gestation she presented with severe recurrent symptoms, suicidal ideation and desire to terminate the pregnancy. Domperidone was offered as a therapy of last resort. The patient was informed of the drug's risks and benefits, lack of FDA approval, and limited safety data in pregnancy. After obtaining the patient and obstetrician's consent, oral domperidone 10 mg every 8 hours was started. The patient did well and had no extrapyramidal symptoms. She was discharged on oral ondansetron and domperidone for hyperemesis and as needed lorazepam for anxiety. She resumed a regular diet and gained weight. At 34 weeks gestation she delivered healthy male infants.

**Discussion:** The goals of treating HG are to maintain fluid and electrolyte balance, maintain caloric intake and control nausea and vomiting. Anti-emetics with IV hydration ± parenteral nutrition may be required. Phenothiazines and anti-histamines are first-line therapy. Metoclopramide is also used; however, its use is limited by central nervous system toxicity. In refractory cases, ondansetron has been used. Domperidone is a gastroprokinetic and anti-emetic. In the US, it is not approved by the FDA due to case studies of arrhythmias, cardiac arrest, and sudden death with IV use. However, oral domperidone can be obtained from abroad and from compounding pharmacies. Our report illustrates the use of domperidone for intractable HG to avoid termination of pregnancy. In women with severe symptoms who are refractory or intolerant to standard therapy, oral domperidone may allow the continuation of pregnancy. We present this case to inform physicians of the potential use of domperidone for severe HG with the understanding that it is not FDA approved and not widely available in the US.

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**An Unusual Path to the Diagnosis of Crohn's Disease; from Gastric Outlet Obstruction to Fat Wrapping of the Terminal Ileum**

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**Purpose:** Crohn's Disease (CD) affects all portions of the GI tract. In familiar presentations, the diagnosis can be challenged by non-diagnostic histology and overlapping features. Thus, when CD presents atypically, a multifaceted approach, with surgeons, radiologists, pathologists, and gastroenterologists is needed to verify the diagnosis and initiate proper therapy. We report a rare presentation of CD, with suggestive endoscopic, radiologic, and histologic findings that, required a virtually pathognomonic laparoscopic feature to verify the diagnosis.

**Case:** A 22 yo man with previous dyspepsia came to the GI clinic after 3 months of vomiting, early satiety, and a 25 lb weight loss. He had no diarrhea, hematochezia, or recent NSAID use. Physical examination was normal, with no evidence of malnutrition. He was PPD negative. EGD revealed gastric outlet obstruction with a large quantity of retained food. EGD after a liquid diet revealed pre-pyloric nodules and erosions with ulceration of the anterior wall of the duodenal bulb resulting in edema and stenosis. On histology, there was chronic inflammation, a granuloma and rare H. pylori. Following treatment for H. pylori, a subsequent UGI series with small bowel follow through revealed slow barium transit through the pylorus and wall thickening of both the duodenal bulb and terminal ileum (TI). Colonoscopy with TI intubation uncovered a cobblestone appearance to the mucosa of the TI (severe inflammation and mucosal fibrosis on histology). A third EGD showed unhealed ulcers and continued gastric outlet obstruction. With persistent vomiting, weight loss, dehydration, and an inability to tolerate oral medications, the patient had a gastrojejunostomy. During surgical exploration, fat wrapping of the terminal ileum was noted. Post-operatively, the patient has regained weight, has no difficulty eating and is otherwise well on oral mesalamine.



**Conclusion:** CD presenting with UGI symptoms is rare, especially as a gastric outlet obstruction. Histological evidence of UGI CD can be common, reportedly occurring in 60–70% of patients. Endoscopic evidence, however, is far less common, occurring in 0.5% to 4% of CD patients. This is an unusual presentation of CD that required a multidisciplinary approach to eventually confirm the diagnosis and initiate treatment.

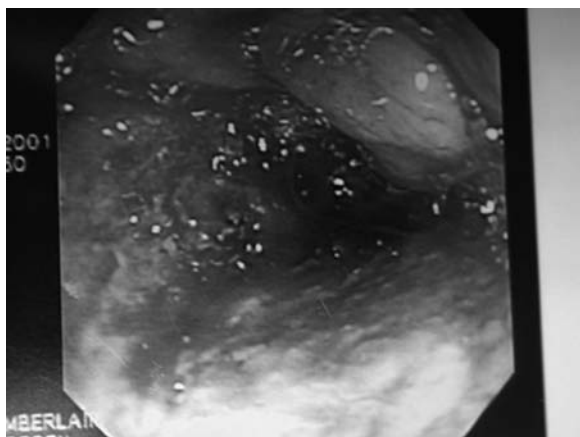
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#### Hemorrhagic Mantle Cell Lymphoma Diagnosed with Colonoscopic Cold Biopsy

Jigneshkumar Patel, MBBS, Subbarmiah Sridhar, MBBS, Sherman M. Chamberlain, MD\*. *Medicine, Medical College of Georgia, Augusta, GA and Section of Gastroenterology, Medical College of Georgia, Augusta, GA.*

**Purpose:** A 62 year old male admitted with constipation, weight loss and rectal bleeding, had a colonoscopy showing active bleeding at the colonic splenic flexure from an extrinsic mass (Fig. 1). With the splenic flexure mass already bleeding, a single cold biopsy was done at the site. Despite the cold biopsy being done, his bleeding stopped spontaneously. CT scan of the abdomen showed thickened colon in the splenic flexure with infiltration of a large 3 cm mesenteric soft tissue component representing either a primary carcinoma or a metastatic tumor (Fig. 2).

**Methods:** Histopathology of the biopsied tissue revealed diffuse infiltrates of atypical lymphoid cells consistent with a B-cell lymphoma. Bone marrow biopsy failed to yield further diagnostic information. The original colonoscopic biopsy was then further evaluated and the patient was diagnosed with a mantle cell lymphoma. The patient's mantle cell lymphoma progressed rapidly despite treatment, and he died within two weeks of his initial presentation.



**Results:** Mantle cell lymphoma represents only 6% of malignant non-Hodgkins lymphomas, and involves the colon in 15–30% of patients. The cold biopsy of the hemorrhagic colonic lesion proved to be critical in diagnosing this patient with mantle cell lymphoma. This case highlights the indication to perform a cold biopsy on a lesion that is already bleeding. Gastrointestinal (GI) hemorrhage risk after cold biopsy is extremely low (0.03–0.14% in prior studies), with no prior study having evaluated the safety of cold biopsy of an already bleeding GI lesion.

**Conclusion:** This is only the third case in the literature of a mantle cell lymphoma presenting with GI hemorrhage. This case illustrates the diagnostic information gained from a cold biopsy of an actively bleeding GI lesion without additional morbidity observed.[figure1][figure2]

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#### An Unusual Case of Hematochezia in a Healthy 28 Year Old Female

Steven R. Fox, MD, Michael C. Duffy, MD\*. *Gastroenterology, William Beaumont Hospital, Royal Oak, MI.*

**Purpose:** A 28-year-old previously healthy female complained of constipation for several months and intermittent hematochezia for one week, noting bright red blood coating her stools. She also noted lower abdominal pain relieved with a bowel movement. She had no fever, chills, weight loss or relationship of symptoms to menstrual periods. Physical exam including a pelvic examination by a gynecologist was normal. The stool was hemoccult positive. Her CBC was normal. A CT Scan of the abdomen and pelvis was normal. Colonoscopy showed a firm, multi lobulated 4 × 5 cm broad-based mass 10 cm from the dentate line that occupied approximately 1/3 of the circumference of the lumen. Biopsies of the mass showed colonic mucosa with changes of mucosal prolapse with foci beneath the muscularis mucosa containing spindle-shaped cells and in one section a small endometrial-type gland indicative of endometriosis. Immunoperoxidase staining showed CD10 positive and C-KIT negative cells consistent with endometriosis. The patient has been referred to a gynecologist specializing in management of endometriosis and is scheduled for laser ablation and/or excision.

**Conclusion:** It is estimated that 4–17% of all menstruating women have endometriosis, with 3–34% of these cases involving the gastrointestinal tract. The rectum and rectosigmoid junction account for 70–93% of all intestinal endometriosis. Colonic mucosal implants are unusual and the disease is rarely diagnosed by endoscopic biopsy. Although most gastrointestinal endometriosis is asymptomatic, symptoms may include abdominal pain, dyschezia, tenesmus, vomiting, diarrhea, constipation, melena or hematochezia. Symptoms do not always correlate with the menstrual cycle. Endometriosis is thought to result from retrograde menstruation leading to implantation on the peritoneum, pelvic viscera, small bowel or colon with occasional invasion through the submucosa. Gastrointestinal endometriosis may be difficult to diagnose, especially if there is absence of mucosal involvement. The differential diagnosis includes infection, ischemia, malignancy and IBD. Treatment may involve hormonal manipulation or segmental resection, particularly with obstructing lesions. We present a case of gastrointestinal endometriosis presenting with constipation and hematochezia in a 28-year-old female diagnosed by colonoscopy and mucosal biopsy. Gastroenterologists should be aware of mucosal endometrial implants as a potential cause of rectal bleeding in young women.

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#### Botulinum Toxin Injection for the Treatment of Gastric Stasis in Patients with Prior Gastric Surgery

Steven R. Fox, MD, Laith H. Jamil, MD, Tusar K. Desai, MD\*. *Gastroenterology, William Beaumont Hospital, Royal Oak, MI.*

**Purpose:** We report three cases in which Botox injection just distal to the gastro-enteric anastomosis led to clinical improvement and objective radiologic evidence of improved gastric emptying in patients suffering from nausea and vomiting after gastric surgery.

**Case 1:** A 48-year-old male presented with 3-months of nausea and vomiting. Upper endoscopy demonstrated pyloric stenosis that could not be traversed. The patient failed medical therapy and required a pyloroplasty with truncal vagotomy. Post operatively the patient continued to have nausea and vomiting, despite parenteral metoclopramide and avoidance of narcotics. UGI x-ray showed delayed gastric emptying and marked distention. Botox was injected at the surgical site. Repeat UGI x-ray showed improvement in gastric distention and emptying. Fourteen weeks after Botox injection the patient was symptom free.

**Case 2:** A 46-year-old female with a history of nausea, vomiting and pyloric stenosis underwent a pyloroplasty and vagotomy. After her surgery she had persistent symptoms. During EGD, Botox was injected at the surgical site which led to improvement in symptoms and the gastric emptying study (Table 1).

**Case 3:** A 63-year-old female presented with complaints of daily nausea and vomiting after vagotomy and Roux-en-Y gastrojejunostomy in 1994. The patient had failed medical therapy. Initial EGD demonstrated a phytobezoar, with a normal anastomosis. Botox was injected at the surgical site. She has reported vomiting less than 3 times a month since the Botox treatment. This has remained constant for the 24 weeks since her therapy. The patient had gastric emptying studies 14 months before, 2 weeks, and 22 weeks after Botox therapy (Table 2).

**Conclusion:** Botox injection just distal to the gastro-enteric anastomosis improves symptoms of nausea, vomiting and objective parameters of gastric emptying. Further prospective studies should be considered.

Gastric emptying study after Botox injection

Gastric emptying	% retained prior to Botox injection	% retained 1 week after Botox injection	% retained 8 weeks after Botox injection
Hour 1	105%	96%	99%
Hour 2	89%	89%	88%
Hour 4	86%	84%	65%

Egg substitute labeled with Technetium-99 m sulfide

Gastric emptying study after Botox injection

Gastric emptying	% retained prior to Botox injection	% retained 2 week after Botox injection	% retained 22 weeks after Botox injection
Hour 1	100%	38%	41%
Hour 2	101%	30%	30%
Hour 4	97%	18%	2%

Egg substitute labeled with Technetium-99 m sulfide

multiple small and large polyps. The small polyps were removed with snare electrocautery. Two erythematous folds were visualized by the standard optical filter at 65 and 57 cm. The NBI system revealed extensive gyrus-like sessile segments of irregular-appearing mucosa. Both lesions were removed by the saline methylene blue elevation technique. Histopathology of both specimens revealed SSAs with focal inverted growth patterns. If the NBI system had not been used, the endoscopist would have chosen to biopsy the lesions, which may or may not have provided enough tissue to identify SSAs on histopathology. Follow-up colonoscopy 3 months later revealed no abnormalities.

**Discussion:** Sessile serrated adenomas superficially resemble left-sided hyperplastic polyps but differ by displaying (1) a higher proliferation index, (2) dilated crypt architecture, (3) serrations extending to the base of crypts and (4) an usually right-sided location. These polyps have been termed “adenomas”, even though they lack conventional cytologic dysplasia and differ from traditional serrated adenomas. They are newly recognized and believed to be precursors of sporadic colorectal cancers with mismatch repair defects. This case illustrates the potential of the NBI technology to increase the yield of significant polyps, including the subtle SSAs—making colonoscopy a more effective tool in colorectal cancer prevention.

## 518

### Achalasia Cardia in an Adult with Acute Renal Failure, Lung Abscess and Spontaneous Pneumomediastinum, a Rare Combination

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**Purpose:** A 24 year old African American male with no significant past medical history, presented with generalized weakness, cough with brownish sputum, weight loss of 10 lbs over a period of 2–3 weeks. He complained of nausea and 3–4 episodes of nonbloody vomiting since 1 week. The patient denied fever, chills, night sweat, chest pain, shortness of breath or palpitations. On examination, Vitals were stable, he was thin and cachectic. Chest was clear and pericardial friction rub was heard. Laboratory exam showed WBC 37.5, Hb/Hct 14.7/43.9, Platelets 598, neutrophils 92%. Chemistry: Na+ 126, K+ 3.9, Cl- 67, HCO3 22, BUN 225, Creatinine 15.6. Chest X-Ray revealed a big cavity with air fluid level compatible with abscess in right lung. He was started on vancomycin and Zosyn for lung abscess and received hemodialysis for uremic pericarditis. BUN and Creatinine came down to 151/8.6 next day. CT Scan of chest revealed pneumomediastinum, markedly dilated esophagus with air and fluid and a large abscess in right

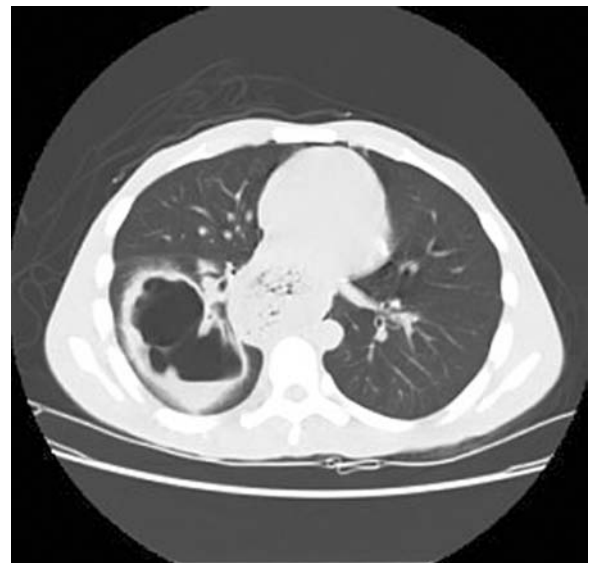
## 517

### Narrow-Band Imaging in the Identification of Sessile Serrated Adenomas

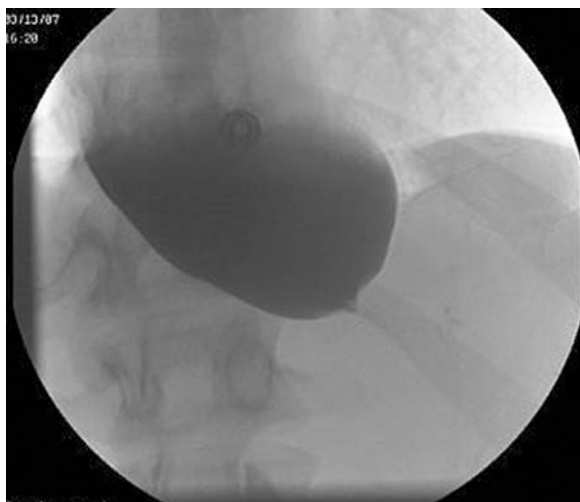
Manuel Y. Lam, BA, Edward Feller, MD, Baishali Bhattacharya, MD, Samir A. Shah, MD\*. Department of Medicine, Warren Alpert Medical School of Brown University, Providence, RI.

**Purpose:** The narrow-band imaging (NBI) system complements conventional colonoscopy in detecting clinically relevant polyps. Sessile serrated adenomas (SSA) are important, often subtle, pre-cancerous polypoid lesions. To demonstrate the clinical utility of NBI, we describe two SSAs identified by this technology during colonoscopy.

**Case:** A 53-year-old man had a screening colonoscopy in 2003, revealing several polyps and an elevated adenomatous area at 50 cm. The latter was not removed completely. Follow-up colonoscopy in 2005 showed sessile polyps at 50 cm; one was marked with India ink. Biopsies showed several hyperplastic polyps and one tubular adenoma. In 2007, the patient was referred to a new gastroenterologist (SAS) overdue for repeat colonoscopy. Past medical and family history were unremarkable, except that his father had “polyps” in his fifties. Physical exam was benign. Conventional colonoscopy showed



lung. Gastrografin esophagogram revealed markedly dilated esophagus with smooth tapering distally and no evidence of contrast extravasations. Upper GI Endoscopy revealed hugely dilated esophagus filled with 1.5 liters of fluid, highly suspicious for vigorous achalasia. Esophageal biopsy ruled out any evidence of malignant infiltration and Pseudoachalasia. Bronchoscopy performed which ruled out any tracheoesophageal fistula and perforation. He improved gradually with the resolution of the renal failure. He was discharged on Clindamycin with manometry to be scheduled as out patient. He was much better at follow up in 1 week with significant weight gain awaiting manometry till we write this case.[figure1][figure2]



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### Rectus Sheath Hematoma Following Large Volume Paracentesis

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**Introduction:** Large volume paracentesis is an accepted method of managing refractory ascites in patients with cirrhosis. We report the case of a major hemorrhagic complication of large volume paracentesis with formation of large rectus sheath hematoma.

**Case:** 57-year-old Caucasian Male with cirrhosis due to Hepatitis C presented for large volume paracentesis for refractory ascites. His INR was 2.3 and hemoglobin was 12 g/dl. Abdominal ultrasound to mark the site for paracentesis revealed large ascites in the left lower quadrant. Approximately 8.5 L of straw-colored ascitic fluid were removed from the marked site. Soon after the procedure, the patient started bleeding from the puncture site to which pressure and a suture were applied. The patient also complained of severe abdominal pain and became hypotensive. He was therefore resuscitated with intravenous fluids and blood products as repeat hemoglobin was 7.9 g/dl. A CT of the abdomen and pelvis showed a large left rectus sheath hematoma (see figure) extending from the level of thoracic cage to pubic symphysis. The patient was managed conservatively and remained hemodynamically stable after initial resuscitation. A repeat CT of the abdomen 4 days later showed a decrease in the size of the hematoma. The development of contrast-induced nephropathy complicated his hospital course. He was discharged to hospice.

**Discussion:** Bleeding as a complication of paracentesis occurs in less than 1% of cases even in the presence of significant coagulopathy and thrombocytopenia. No data exists to support a cutoff value for coagulation parameters beyond which paracentesis should be precluded. Routine correction of prolonged INR and thrombocytopenia before abdominal paracentesis is not recommended. Conservative management including fluid resuscitation, correction of coagulopathy and blood transfusion is recommended in such cases.

Invasive measures including therapeutic angiography with embolization and surgical exploration are reserved for patients who fail conservative measures. It is important to recognize the existence of this serious complication as awareness may accelerate the diagnostic process and treatment.[figure1]



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### Diagnosis of Shwachman-Diamond Syndrome in a 24-Year-Old Woman with Abdominal Pain and Fatty Replacement of the Pancreas

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Shwachman-Diamond Syndrome (SDS) is genetic disease characterized by pancreatic insufficiency, fatty replacement of the pancreas, and neutropenia. It typically presents in childhood, however we describe the diagnosis of SDS in a young woman presenting with abdominal pain.

**Clinical Presentation:** A 24-year-old woman presented with post-prandial abdominal pain, relieved with defecation. The physical exam was normal. Laboratory evaluation was significant for a WBC of 2400, a platelet count of 150,000 and a hematocrit of 37.

**Evaluation:** Further review of pediatric records revealed a history of cyclic neutropenia and childhood failure-to-thrive. An abdominal CT scan showed abnormal enhancement of the pancreas, consistent with complete fatty replacement. Serum trypsin was <1.2 (normal is 10–57), suggesting pancreatic insufficiency. A spot sudan stain for fecal fat was normal. Sweat test and CFTR gene mutation testing for cystic fibrosis were normal. Genetic testing revealed a mutation in the SDS gene on chromosome 7, confirming a diagnosis of SDS.

**Differential Diagnosis:** The differential diagnosis of pancreatic exocrine insufficiency in a young person with no alcohol history includes hereditary hemochromatosis, alpha-1 antitrypsin deficiency, pancreatic neoplasm, malnutrition, diabetes and cystic fibrosis. Rarer genetic disorders in children include a mitochondrial disorder called Pearson Syndrome, an ectodermal dysplastic disorder called Johanson-Blizzard Syndrome, and SDS. Of these disorders only diabetes, cystic fibrosis and SDS cause extensive fatty replacement of the pancreas.

**Discussion:** SDS is caused by a deficiency in an aspect of RNA metabolism essential for the development of the exocrine pancreas, hematopoiesis and chondrogenesis. The disease usually presents in childhood with growth delay, diarrhea and recurrent infections due to cyclic neutropenia. Pancreatic insufficiency often improves with age, but can be identified by a low serum trypsinogen or isoamylase level, which may continue to be abnormal even when steatorrhea resolves. Genetic testing is available to confirm the diagnosis of SDS, however a negative test does not rule out the disorder. As

SDS can be complicated by life-threatening neutropenia, thrombocytopenia, leukemia and aplastic anemia, hematology follow-up is essential.

**Conclusion:** A diagnosis of SDS should be considered in young patients who present with vague GI complaints, leukopenia, and fatty replacement of the pancreas.

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#### Experience Using Nitazoxanide in a U.S. Genotype 1 Hepatitis C Patient

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Hepatitis C is the most common chronic bloodborne viral infection in the United States. It is estimated that 3.9 million (1.8%) of Americans have been infected with Hepatitis C of which 2.7 million are chronically infected. Standard treatment today consists of a pegylated alpha interferon (peg-IFN) in combination with ribavirin (RBV) for 24 to 48 weeks. The goal of therapy is to clear the hepatitis C virus (HCV) RNA as measured by PCR and to attain a sustained viral response after treatment is stopped. However, it is now reported that a quarter of Americans living with HCV have failed standard treatment. This has opened the door to search for new treatment regimens that may be beneficial in treating this disease.

Rossignol, et. al. presented a poster "Nitazoxanide in Treating Chronic Hepatitis In Vitro Activity and Clinical Case Series" at Digestive Disease Week 2006. This poster detailed the in vitro antiviral properties of nitazoxanide and included several clinical case reports in treating HCV in Genotype 4 patients. Nitazoxanide's outstanding safety profile was confirmed in all hepatitis C infected patients.

Case report detailing an experience using nitazoxanide along with peg-IFN in treating HCV in a Genotype 1 patient utilizing the same protocol that was used in the genotype 4 trial referenced above. Safety parameters, including liver enzymes and HCV RNA levels via PCR were also monitored.

This patient is a 52 year old male, genotype 1, which was naïve to any treatments. The patient was started on nitazoxanide 500 mg twice a day on February 1, 2007. At this time, his HCV RNA was 15,300,000 IU. All other laboratory parameters were within normal limits (WNL). On April 12, 2007 (approx. 10 weeks post induction) peg-IFN was added to the nitazoxanide. After four weeks of combination therapy, the patient HCV RNA was 100,000 IU. Thus, the patient had a greater than 2 log reduction in his HCV RNA. No adverse events have occurred and all other laboratory parameters are within normal limits. I will continue to treat and monitor this patient in order to complete the 48 weeks of nitazoxanide and peg-IFN.

This case report details an experience with nitazoxanide induction therapy followed by a combination of nitazoxanide along with pegylated alpha interferon (peg-IFN  $\alpha$  2a) in a genotype 1 patient with compelling results. Although this result has shown great promise, larger, randomized trials need to be conducted in U.S. to confirm and expand upon this finding.

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#### Development of Lymphomatoid Papulosis in a Patient with Crohn's Disease Treated with Infliximab — A Case Report

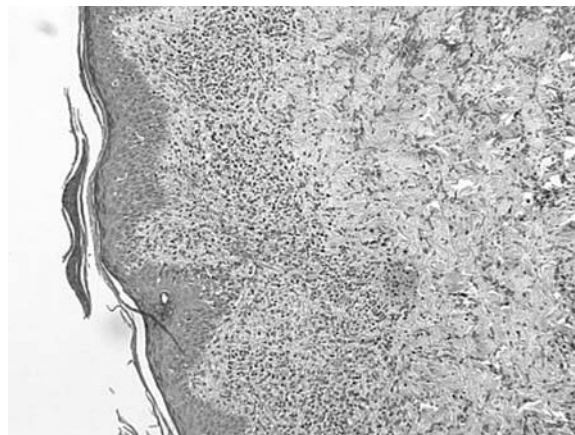
William Outlaw, MD, Alan Fleischer, MD, Richard Bloomfeld, MD\*. Gastroenterology, Wake Forest University, Winston-Salem, NC and Dermatology, Wake Forest University, Winston-Salem, NC.

A 21 year-old white male was diagnosed with ileocolic Crohn's disease at age 8. His disease course was complicated by perianal abscess and fistulae at age 11. Ultimately, he was well on a regimen of azathioprine (150 mg daily) and infliximab (5 mg/kg IV every 12 weeks) immediately prior to starting college. Eventually, he developed progressive abdominal pain associated with anorexia and a 10-pound weight loss. Scattered violaceous papular nodules erupted on his extremities and buttocks (Fig. 1). A course of prednisone improved his pain and appetite, but not his rash. Biopsies of the rash were consistent with lymphomatoid papulosis (Fig. 2). Remicade was discontinued. He declined methotrexate, so azathioprine was continued

for maintenance of remission. He remains clinically well and his rash has improved.

Lymphomatoid papulosis (LP) is a rare (incidence <2 per one million population) cutaneous lymphoproliferative disorder characterized by activated T-cells (usually CD30+). The skin lesions of LP typically are < 3.0 cm in diameter and usually come and go spontaneously. Overall survival is excellent, approaching 100% over 5 years. Nevertheless, up to 20% of patients with LP may progress to cutaneous lymphoma (such as anaplastic large T-cell lymphoma or mycosis fungoides) and there is a 50% cumulative risk of developing cutaneous lymphoma 25 years after the initial diagnosis of LP is made.

LP is most frequently reported in immunocompromised patients, especially those with solid organ or bone marrow transplantation. A LP-like eruption has been described in one patient on anti-TNF therapy (adalimumab) for rheumatoid arthritis. To our knowledge, this is the first report of LP in a patient with Crohn's disease on infliximab.[figure1][figure2]



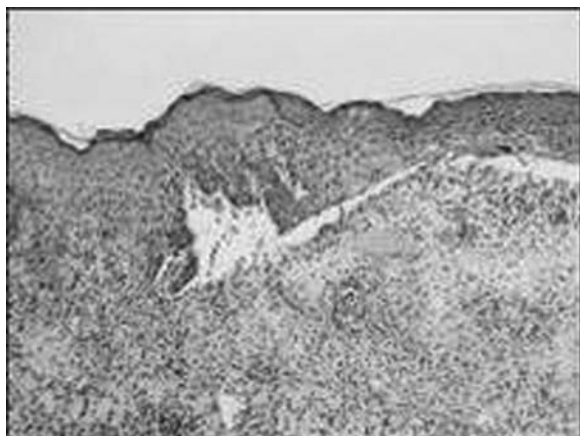
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#### Steroid Unresponsive Sweet's Syndrome in a Patient with Crohn's Disease

Christopher D. Gamble, MD\*, Prema R. Menon, MD. Internal Medicine, Ball Memorial Hospital, Muncie, IN.

Sweet's Syndrome, or acute febrile neutrophilic dermatosis, is a condition characterized by the sudden onset of fever, leukocytosis, and tender, erythematous, well-demarcated papules and plaques which show dense neutrophilic infiltrates on histologic examination. Although it may occur in the absence of known disease, Sweet's Syndrome can occur with diseases such as Leukemia, Rheumatoid Arthritis, and Inflammatory Bowel Disease. A 34 year old female presented with an exacerbation of Crohn's Disease and

was treated with steroids, fluid rehydration, anti-emetics, pain medication and azathioprine. On day 5 of hospitalization she was noted to have a low grade temperature, moderate leukocytosis and a burning, non-pruritic rash. Scattered vesicles were present on her face, neck, both sides of the upper chest and back, both lower extremities and the proximal phalanx of her left middle finger. Some vesicles had central areas of necrosis and one of her fingers demonstrated a violaceous necrotic plaque. A biopsy revealed a neutrophilic pustular dermatitis and a diagnosis of Sweet's Syndrome was made. Despite treatment with a number of therapies to include colchicine, prednisone, and infliximab, her rash as well as her Crohn's symptoms continued to worsen. Having failed medical therapy for both her Crohn's Disease and Sweet's Syndrome, she ultimately underwent a proctocolectomy, which subsequently brought about complete resolution of her GI symptoms and skin lesions. A literature search failed to reveal a similar case in which a patient with Crohn's Disease and Sweet's Syndrome who failed medical therapy had such a profound response to surgical therapy. Our case prompts the idea that patients with Crohn's Disease and Sweet's Syndrome who do not respond to medical therapy may benefit with regards to overall morbidity with early surgical intervention. Further investigation is warranted.[figure1][figure2]



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### Acute Liver Dysfunction after Addition of Natalizumab to Interferon in Two Patients with MS

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Interferon-beta (IFN $\beta$ ) and natalizumab are commonly employed therapies for multiple sclerosis. IFN $\beta$  has been associated with rare hepatotoxicity, including autoimmune hepatitis in several patients. To date, serious hepatotoxicity has not been reported with natalizumab use. Here, we describe two patients with MS who developed autoimmune hepatitis shortly after being initiated on natalizumab.

**Case #1:** A 26 y/o woman was admitted due to new onset of jaundice and fatigue. Her MS had been treated with interferon-beta-1a. This was discontinued two weeks prior to her presentation because of the development of a rash. One week prior to her presentation natalizumab was given for her MS. Initial laboratory data included an INR of 2, total bilirubin of 4.6 mg/dL, AST of 1863 U/L, ALT of 2212 U/L, and alkaline phosphatase of 74 U/L. Liver biopsy revealed centrilobular necrosis, lobular disarray with ballooning degeneration, mild canalicular cholestasis, and minimal microsteatosis (see image 1) thought consistent with AIH.

**Case #2:** A 52 year-old woman with MS presented to the hospital with jaundice and abdominal pain. The patient's MS had been treated for several years with interferon-beta-1a and methotrexate. Three months prior to admission, natalizumab 400 mg was initiated intravenously on a monthly basis for worsening symptoms. After the second dose of natalizumab, the patient was noted to have an asymptomatic elevation in her liver function tests and methotrexate was discontinued. Shortly after the third dose of natalizumab, she developed jaundice and worsening right upper quadrant abdominal pain. Laboratory data was significant for a total bilirubin of 6.6 mg/dL, AST 1984 U/L, ALT 1548 U/L, alkaline phosphatase 256 U/L, IgG 1860 mg/dL, anti-nuclear antibody 1:640 titer, and INR of 1.3. Liver biopsy revealed chronic hepatitis with marked portal inflammation with prominent plasmacytic infiltrate consistent with autoimmune hepatitis (see image 2).

**Discussion:** In this report, we describe two cases of autoimmune hepatitis following the administration of natalizumab for treatment of MS. Based on these reports, we would strongly suggest that liver function testing be closely monitored in all patients for evidence of acute hepatitis and liver dysfunction during treatment with natalizumab.

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### Bariatric Surgery in Patients with Crohn's Disease and Extreme Obesity

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The clinical course and severity of Crohn's disease in obese patients is characterized by more disease activity and more frequent peri-anal complications. The aim of this study was to determine the impact of bariatric surgery and subsequent weight loss on the course of Crohn's disease in two patients with extreme obesity.

Following IRB approval, patients were identified in the Mayo Clinic records with the following characteristics: extreme obesity, defined as a BMI greater than 40; Crohn's disease, documented by the usual clinical criteria; and bariatric surgery for treatment of secondary complications of obesity. Data was recorded retrospectively.

Two patients, both female, were identified. Both had Crohn's disease with ileo-colonic and perianal involvement, and both were taking azathioprine for maintenance of remission. Both had a history of lower extremity DVT and

obstructive sleep apnea. At the time of bariatric surgery, Patient #1 was age 37, weight 165 kg, and her BMI was 68.7. She had undergone one resection of 20 cm of ileum, 16 cm of cecum and ascending colon, and 12 cm of sigmoid colon for Crohn's disease refractory to medical therapy. She had been in symptomatic remission for 14 mo prior to bariatric surgery. Patient #2 was age 47, her weight 182.3 kg, and BMI 58.9. She had not undergone surgery for Crohn's disease. She had been in symptomatic remission for 18 mo prior to bariatric surgery. The patients had not taken corticosteroids for Crohn's disease for 15 mo and 12 mo, respectively. Both had proximal gastric stapling with Roux en Y gastric bypass. The post-op course in Pt #1 was complicated by hypotension and in Pt #2 by respiratory acidosis requiring intubation and mechanical ventilation. Both required re-hospitalization for nausea and vomiting, and Pt #1 had a wound infection. Patients #1 and #2 lost 20 kg and 73 kg, respectively, by the 10th & 12th month post-op, respectively, with reductions in BMIs to 62 and 34.8, respectively. The Crohn's disease remained in symptomatic remission, on azathioprine, in both for the duration of follow-up.

Gastric stapling and bypass was safe and beneficial in two patients with Crohn's disease and extreme obesity. Neither patient experienced a flare of Crohn's disease following surgery.

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**Gastrointestinal CMV Disease in an Immunocompetent Host**

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Gastrointestinal CMV is a well-described problem in patients who are immunocompromised. Rarely, gastrointestinal CMV can also affect immunocompetent patients. Here we report an immunocompetent patient with gastrointestinal CMV disease, and we discuss when to treat such patients with antivirals.

An 83 year-old immunocompetent male with diabetes presented for black stool. EGD and colonoscopy showed antral ulcers, a duodenal ulcer, and scattered colonic ulcers. Biopsies came back positive for gastric, duodenal, and colonic CMV. The patient was referred to immunology whose initial impression was that the CMV was an innocent bystander. It was decided not to treat the CMV. He had no further melena. However, a repeat EGD and colonoscopy ten months later showed persistence of the CMV. A Medline search focusing on when to treat with antivirals in an asymptomatic immunocompetent patient with CMV was done.

Most CMV disease occurs in patients immunocompromised by HIV, organ transplants, chronic steroids, or chemotherapy. CMV disease is exceptionally rare in the immunocompetent, being the subject of only a few case reports. Gastrointestinal CMV most often presents as diarrhea, abdominal pain, and bleeding. Treatment is usually with ganciclovir, but immunocompetent patients are often not treated with antivirals. A meta-analysis of cases of CMV colitis in immunocompetent hosts in *Digestive Diseases and Sciences* by Gaiatsatos and colleagues found that there was a higher mortality in patients of male gender who were older than 55 and in patients with chronic diseases. Among patients younger than 55, 50% had spontaneous resolution without antivirals, and survival for their group was 100%. However, in those older than 55, only 32% had spontaneous resolution, and survival for their group was 45%. Since our patient was both a male older than 55 and also a diabetic, we treated him with a course of oral ganciclovir. A followup colonoscopy was normal, but EGD showed persistence of the duodenal ulcer with CMV present in the biopsies. Re-treatment with IV ganciclovir is currently being pursued.

Here we present a case of gastrointestinal CMV in an immunocompetent patient, and we discuss reasons to treat with antiviral therapy versus observation. The available literature supports the use of antivirals in patients older than 55 or with co-morbidities.

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**The Use of Infliximab To Treat a Patient with Both Familial Mediterranean Fever and Crohn's Disease**

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A 23-year old cigarette smoker of Ashkenazi Jewish descent developed abdominal pain, diarrhea and bloody stools. He did not have fevers, back pain, nausea or vomiting. A colonoscopy showed aphthous erosions throughout the entire colon, and biopsies revealed cryptitis with crypt abscesses and some architectural distortion consistent with a diagnosis of Crohn's disease (CD). Mesalamine therapy was not effective while treatment with prednisone showed prompt improvement. However, prednisone tapering was unsuccessful and his abdominal pain and hematochezia reoccurred.

The patient came to our center for a second opinion of his CD. Repeat colonoscopy and biopsies confirmed the diagnosis of CD of the colon, and a CT scan revealed distal ileal thickening. Azathioprine therapy resulted in hepatitis and profound nausea. During his two year evaluation and treatment for CD, he developed intermittent right-sided pleuritic chest pain. Distinct episodes lasted 1–2 weeks every 2 months and often required ER visits for analgesia. A thorough work-up with a CT scan and evaluation for pulmonary embolus were negative. Genetic testing revealed that the patient had Familial Mediterranean Fever (FMF). Treatment with colchicine improved his pleuritic and abdominal pain, but resulted in treatment-limiting diarrhea. He was then treated with infliximab (5 mg/kg induction and q 8 week maintenance) with prompt resolution of all his symptoms and successful steroid tapering. At 14 months follow-up, he has not had further pleuritic symptoms and is in stable remission of his CD.

FMF is most commonly seen in Turkish, Sephardic Jewish and Arabic populations. The disease is less commonly seen in Ashkenazi Jews, with an FMF carrier frequency of 1 in 135 and a disease prevalence of 1 in 73,000. Interestingly, both the FMF gene (MEFV) and the CD susceptibility gene CARD15 are located on chromosome 16. It has been proposed that inflammation induced by FMF provokes expression of other inflammatory diseases in genetically predisposed patients. Co-existing CD and FMF is rarely reported. Infliximab therapy was used for this patient's steroid-dependent CD but the additional benefit of control of his FMF was not anticipated. The current mainstay of FMF treatment is colchicine therapy that is limited by diarrhea and GI upset. TNF- $\alpha$  has been thoroughly described in the pathogenesis of CD and has also been shown to upregulate the MEFV gene in FMF. The results of this case suggest that patients with co-existing CD and FMF may benefit from monotherapy with infliximab.

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**FISH-ing for the Correct Diagnosis**

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A twenty year old morbidly obese African American female status-post gastric bypass in 2003 presented to the emergency department complaining of chest pain and increasing shortness of breath. Spiral CT of the chest was performed as part of her larger work-up that was negative for PE, but revealed a large heterogeneous appearing mass occupying and enlarging the left lobe of the liver with a single 5 cm mass in the right lobe with peripheral enhancement. The only risk factor for viral hepatitis was home tattooing. Labs were essentially normal including AFP and a negative viral hepatitis profile. CT guided liver biopsy was performed with the initial interpretation of metastatic thyroid carcinoma to the liver based mainly on the morphologic appearance that showed a follicular/glandular pattern with a homogenous eosinophilic material within the lumen. No hepatic tissue was identified within the biopsy. Second opinion subsequently ruled out thyroid carcinoma based on negative TTF-1 and thyroglobulin stains. Patients care was transferred to two additional institutions that assisted in making a diagnosis. A second biopsy was suggestive of hepatoblastoma or possibly cholangiocarcinoma, but no definitive diagnosis was ever made. Her last set

of biopsies were extensively reviewed by our in house pathology service and again a second opinion was requested to confirm the diagnosis in this problematic case. The tumor is focally keratin positive (including CK7) with strong synaptophysin and focal chromogranin positivity, with corresponding negative HepPar1, AFP, desmin, and S100. The main differential diagnosis based on the morphologic appearance and immunohistochemical staining was neuroendocrine carcinoma or Ewing's sarcoma/PNET. To definitively distinguish between the two a FISH (Fluorescence In Situ Hybridization) was performed on the block for the t(11;22)(q24;q12) translocation which is found in approximately eight-five percent of patients with Ewing's sarcoma. No translocation was identified supporting the diagnosis of neuroendocrine carcinoma. Further work-up to search for a primary extrahepatic lesion was pursued and negative. Due to patient's tumor burden, she was not a candidate for surgical resection. Patient was recently started on a chemotherapy protocol of cisplatin and irinotecan.

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### Duodenal Variceal Hemorrhage Treated with TIPS

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Duodenal varices are uncommon in patients with cirrhosis when compared to esophageal and gastric varices. Hemorrhage from duodenal varices is rare and treatment is not well documented. We describe a case of bleeding from duodenal varices in a patient with cirrhosis successfully treated with a transjugular intrahepatic portosystemic shunt (TIPS).

A 67 year-old Caucasian female with alcoholic cirrhosis presented to an OSH with bright red blood per rectum. An extensive evaluation including an EGD, colonoscopy, wireless capsule endoscopy, and enteroscopy did not locate the source of the bleeding. A tagged-RBC scan localized a potential source involving the small intestine. A diagnostic laparoscopy with assisted enteroscopy was negative. The patient had continued bleeding, requiring >30 units of pRBC over a four month period.

Upon presentation to our institution, the patient continued to have bright red blood per rectum. An EGD revealed a normal esophagus without varices. The gastric mucosa showed evidence of portal hypertensive gastropathy without varices. In the second portion of the duodenum, bulbous lesions were actively oozing blood (see Fig. 1). Miniprobe ultrasonography revealed serpiginous hypoechoic lesions with blood flow consistent with varices.

A RUQ ultrasound revealed patent liver vasculature. A TIPS was placed. The portal gradient was reduced from 19 mmHg to 6 mmHg following TIPS. Collateral blood flow noted pre-procedure was obliterated.

Following TIPS, the GI bleed stopped. The patient did well after TIPS without encephalopathy and was discharged after liver transplantation evaluation. At five month follow-up, the patient denied any further bleeding.

We present a case of duodenal hemorrhage in the setting of cirrhosis. It is a rare etiology for GI hemorrhage that can be successfully treated with TIPS.

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### Type III Choledochal Cyst Variant: First Description of a "Closed Choledochoceles" with Biliary and Pancreatic Drainage Via the Accessory Duct

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Type III choledochal cysts, also called choledochoceles, are rare congenital or acquired malformations of the terminal biliary tree of unknown etiology. These cysts can predispose a patient to biliary colic, obstructive jaundice, or idiopathic recurrent pancreatitis through an obstructive mechanism as the normal flow of bile is disrupted. They have been described in two anatomic variants 1) both the pancreatic and bile ducts drain into the choledochocoele 2) the choledochocoele is a cystic outpouching into the duodenum proximal

to a normal ampulla. Endoscopic ultrasound and ERCP are primary tools to help diagnosis these anomalous formations and needle-knife sphincterotomy has recently been used to treat these cysts in symptomatic patients. We report the case of a 23 year-old white female with no previous past medical history who developed acute pancreatitis two weeks after completing an unremarkable first pregnancy. On EUS, she was found to have a Type III choledochocoele with no apparent drainage into the duodenum. Bile was seen draining from the accessory duct. Subsequent ERCP via the minor papilla revealed communication of the ventral pancreatic and common bile ducts within a choledochocoele which did not communicate with the duodenum. The bile duct appeared to empty retrograde into the ventral pancreatic duct and subsequently out to the duodenum via the accessory duct. To facilitate biliary and pancreatic duct drainage, the choledochocoele was accessed and opened with a needle-knife followed by biliary sphincterotomy and temporary plastic biliary stent placement. Six weeks following the procedure, she continues to feel well. This case represents the first description of a "closed choledochocoele" with biliary and pancreatic drainage via the accessory duct.[figure1]



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### Pancreatic Sarcoidosis Diagnosed by EUS with FNA

Kevin S. Jo, MD, William Shaheen, MD, Asad Ullah, MD, Ashok Shah, MD\*. Gastroenterology and Hepatology, University of Rochester, Rochester, NY.

We present a case of pancreatic sarcoidosis in a patient with painless jaundice and a pancreatic mass. Definitive diagnosis was obtained by EUS with fine-needle aspiration (FNA) for sarcoidosis, thereby avoiding surgical exploration.

A 39 year-old African American male with a history of neurosarcoidosis developed jaundice and presented for evaluation. The patient denied abdominal pain, nausea, vomiting, and fever/chills. He noted a 100 lb weight loss over the last year that was partly intentional. Furthermore, the patient admitted to pruritis, clay-colored stools, and dark urine color.

Initial laboratory evaluation revealed a total bilirubin 12.3, direct bilirubin 10.3, alkaline phosphatase 311, AST 86, ALT 30, but normal pancreatic enzymes. MRI revealed a 3.7 cm × 4.8 cm × 4.9 cm mass in head of pancreas with peripancreatic lymph node enlargement (Fig. 1). Moderate intrahepatic biliary duct dilatation was noted as well as common bile duct (CBD) and pancreatic duct dilatation. A Ca 19-9 level was elevated at 367 U/ml.

An EUS was performed with FNA. An enlarged hypoechoic pancreatic head pancreas without discrete pancreatic mass was noted. Peripancreatic lymphadenopathy was observed. A #22 gauge needle was used to obtain an FNA of both the pancreatic head and surrounding lymph nodes. An ERCP was then performed which revealed a 3 cm stricture in the distal CBD. A sphincterotomy was performed followed by placement of a 10 French/9 cm CBD stent with resultant bile flow.

Biopsy of the pancreatic head and surrounding lymph nodes was negative for malignant tumor cells. Non-caseating granulomas were identified in both the pancreatic head and LAD. Flow cytometry and bile duct brushing were both negative. The patient was subsequently started on steroids for treatment of his sarcoidosis after rheumatology consultation.

Sarcoidosis involving the pancreas is rare and is often diagnosed incidentally following surgical resection of a periampullary pancreatic mass. We describe a case of pancreatic sarcoidosis presenting as a pancreatic mass concerning for malignancy and diagnosed by EUS with FNA. The use of EUS in obtaining a definitive tissue diagnosis prevented surgical exploration.

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### A Female with a History of Dysfunctional Menstrual Bleeding with an Uncommon Cause of Fe Deficient Anemia

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The purpose of this study was to review an uncommon cause of fe deficiency anemia in a female with dysfunctional menstrual bleeding. 44 year old pt with FHx CRC (father dxed age 52) referred to GI service in regard to history of Fe deficient anemia. Pt also had a history of dysfunctional uterine bleeding and a more recent history of loose stools. The pt was evaluated by GI and scheduled for EGD/Colonoscopy. Pt had stool studies that were negative for fecal wbc and an infectious source. EGD was done and was normal. Colonoscopy was done and showed over 100 polyps (consistent with a polyposis condition/syndrome), sessile and pedunculated, ranging in size from approximately 2 mm to over 15 mm. Colonoscopy was limited to the transverse colon due to increased polyp number and size and near obstruction of the lumen. Biopsies were taken and pt was encouraged to remain on a liquid diet and to go to the ER if any N/V, abdominal pain, or other problem and a surgical referral was placed. Pt was already being seen and evaluated by hematology and oncology for anemia. The biopsy result showed adenocarcinoma at one site and carcinoma in situ at another site. Other polyp biopsies were adenoma and some were hyperplastic in the distal colon. Pt was seen and evaluated by surgery and had abdominal colectomy and ileorectal anastomosis (the distal sigmoid colon and rectum were spared of any mass or large or adenomatous appearing polyps). In addition, pt had TAH/BSO for hx of dysfunctional uterine bleeding and large fibroids (two 4-5 cm uterine fibroids). Pt also being referred for further evaluation for polyposis syndrome for genetic counseling and testing.

Although young and middle aged women with dysfunctional menstrual bleeding can present with fe deficient anemia, gastrointestinal and other causes of anemia should also be considered and evaluated for in this pt population.

## 533

### A Novel Endoscopic Treatment of a Gastric Duplication Cyst

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A 30 year old previously healthy male presented with one week of severe chest burning, diminished oral intake, and fifteen pound weight loss. Exam revealed a non-tender abdomen with left upper quadrant distension. Chest x-ray showed an air fluid level in the left upper quadrant. CT scan showed a markedly distended stomach filled with fluid and a round, thick walled

mass with central fluid density at the pylorus measuring 3.2 by 2.4 by 2.6 centimeters. A nasogastric tube was placed for gastric decompression.

The EGD showed an extrinsic bulge occluding the lumen of the pylorus. 8 cc of clear fluid was aspirated via EUS showing benign columnar mucinous epithelial cells. Provisional diagnosis was gastric duplication cyst.

Endoscopic therapy was undertaken. A needle knife was used to cut through the wall of the pyloric channel and into the duplication cyst. This allowed fluid to drain from the cyst and partially collapse the cyst. The track into the cyst was then dilated with a 10 – 12 mm wire guided CRE balloon. The interior of the cyst was examined with the endoscope and showed a smooth wall with an unremarkable lining. Following this, two clips were placed along the sides of the cut surface to facilitate extension with a needle knife cut. The opening was then further dilated with a 12 – 15 mm CRE balloon.

In order to marsupialize the cyst, the roof was partially excised as follows. A double channel endoscope was introduced. A snare was used to grasp one of the clips and through the second channel a needle knife was used to cut an elliptical piece of tissue around the clip. Hot biopsy forceps were used to control bleeding. The forceps were also used to avulse tissue from the margins of the orifice.

Four weeks post-procedure the patient had regained the fifteen pounds he had lost and had resumed a regular diet. Currently, twenty six weeks since endoscopy the patient continues to maintain his weight on a regular diet.

A duplication cyst is an enteric cystic structure that is in intimate contact with the stomach, sharing with the stomach a common blood supply and all muscle layers. It is often lined by gastric columnar mucosa and it is unusual for a duplication cyst to remain asymptomatic until adulthood. In the past, management of gastric duplication cysts relied primarily on surgical intervention.

## 534

### Eosinophilic Esophagitis in a Patient with Sjogren's Syndrome

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A 63 year-old white female with Sjogren's syndrome complained of recurrent gingivitis, oral mucosal ulcerations, chronic nausea, dyspepsia, and dysphagia for solids and pills. In the past year she had an unintentional 50 pound weight loss and had lost her sensation of taste. In recent months she also developed redness and dryness of her vulva. She had a history of erosive esophagitis and gastritis documented on two prior endoscopies and multiple esophageal dilatations were performed in the past to treat her dysphagia. Her last barium swallow revealed non-specific narrowing of the upper and distal esophagus with no clear Schatzki's ring identified.

On exam was a middle aged white female who was not jaundiced. There was an irregular shaped area of erythema on her right buccal mucosa with white striations in the pattern of Wickham's striae. There were no discrete oral ulcerations. Cardiovascular and respiratory exams were normal. Her abdomen was soft and non-tender with no distention, organomegaly or masses. There was erythema and edema of her external genitalia, particularly of the labia minora, but no genital ulcerations.

EGD revealed a narrow caliber esophagus with areas of friability and desquamation of the mucosal surface. Biopsies from the mid-esophagus were consistent with the diagnosis of eosinophilic esophagitis (>20 eos/hpf). Small bowel biopsies were normal, showing no evidence of celiac sprue.

A minor salivary gland biopsy had confirmed the diagnosis of Sjogren's syndrome.

Cutaneous immunofluorescence was negative and there was no evidence of lupus, vasculitis, or autoimmune bullous disorder. Vulvar biopsies revealed marked acute and chronic inflammation that was non-specific with no eosinophils identified. The patient's oral mucosal findings were typical of Lichen Planus however they resolved before they could be biopsied.

Eosinophilic esophagitis (EE), Sjogren's syndrome (SS) and lichen planus (LP) share a number of interesting features. They are all immune mediated



disorders with an association to either allergens or autoantigens. Gastrointestinal manifestations are also common in all three disorders. Though they share a number of similarities, current knowledge about their pathogenesis supports they are distinct entities. We report our case as an interesting example of a patient with three disorders that, although distinct in pathogenesis, share a number of similarities that may impact her future treatment.

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### Obscure-Overt Gastrointestinal Hemorrhage: A Rare Case of Bleeding Ectopic Ileal Varices Managed by Double Balloon Enteroscopy

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A 63 year-old man was seen for obscure-overt gastrointestinal bleeding. Medical history was pertinent for BPH. There was no history of liver disease, alcohol intake, bleeding diathesis, abdominal surgery, or use of NSAIDs. Since May 2006, the patient had many negative workups for obscure bleeding; including endoscopy, colonoscopy and angiography. A capsule endoscopy was suggestive of a bleeding lesion in the distal ileum. He was transfused 29 units of PRBCs over six hospitalizations. The patient was referred for double balloon enteroscopy (DBE). At initial consultation he was not bleeding. An elective DBE was planned. The following day the patient presented with dizziness and hematochezia. There was no abdominal pain, hematemesis, or chest pain. Vital signs were normal and rectal exam revealed bloody stool. Initial labs were hemoglobin of 9.1, MCV of 74.2. All other labs were normal. The patient was admitted and transfused.

Hematochezia continued requiring 10 units of PRBCs during hospitalization. A transcolonic DBE was performed and no fresh blood was seen through the first 125 cm of the ileum. The most distal extent of the exam was inked. The patient continued to bleed and DBE from above was performed. A small amount of fresh blood was noted in the proximal ileum.

Upon withdrawal of the scope with irrigation, two clusters of varices located in the mid-ileum were noted. A mucosal break with a platelet plug was noted on one varix, suggesting an area of recent bleed.

Cyanoacrylate glue was injected into the varix to ensure hemostasis. The scope was withdrawn slowly without identification of other varices. The patient was monitored closely without bleeding for 72 hours post procedure. The patient was discharged and has remained stable 2 months later.

Ectopic varices describes large portosystemic venous collaterals occurring anywhere in the abdomen except in the cardioesophageal region. Ectopic varices are an uncommon cause of gastrointestinal hemorrhage, and make up 5% of all cases of variceal hemorrhage. The literature on this topic consists of small series and case reports. Therapeutics in this arena are based on expert experience, not on randomized trials. Ileal varices are exceptionally rare, especially in the absence of portal hypertension. We believe our case to be the first case of ileal varices treated at DBE with cyanoacrylate.

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### Methylnaltrexone (MNTX) for Constipation in a Patient on Opioids with Malignant Spinal Cord Compression

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To investigate the effect of MNTX on constipation in a patient (pt) on opioids with malignant spinal cord compression. MNTX is a peripherally acting mu-opioid receptor antagonist. In clinical trials, subcutaneous (SC) MNTX reversed opioid-induced constipation (OIC) in pts with advanced illness (AI) without reversal of analgesia or causing withdrawal.

A 46-yr-old man with metastatic, NSC lung cancer and spinal cord compression was referred to the Palliative Medicine service for upper abdominal and right chest pain. The pt had received numerous chemotherapies as well as

radiation to metastatic lesions from T8 to T10. Surgery for the cord compression was not advised and on admission the pt reported taking MS Contin 100 mg bid and had not had a bowel movement in 3 days. His exam showed paraplegia and muscle wasting of the lower extremities. The impression was that he had chest pain due to a paraspinal tumor and spinal compression. His abdominal pain was felt to be a combination of constipation and paraspinal tumor. The constipation was felt to be due to opioids as well as cord compression. During hospitalization the opioids were optimized. He had been on colace and senna without alleviation of constipation. The pt consented to participate in a trial of SC MNTX in OIC in pts with AI.

Per protocol, the pt was randomized to a double-blind dose of 0.3 mg/kg of SC MNTX. Within minutes, he experienced abdominal cramping. About 50 min after the SC MNTX, the pt had a spontaneous passage of a very large amount of stool. After laxation, his cramping subsided and he reported feeling very much relieved. He also reported improvement in his abdominal pain from 4/10 prior to treatment to 3/10 after the bowel movement. No evidence of opioid withdrawal was noted. The pt received an open-label dose of SC MNTX at 0.15 mg/kg the next day. He again had a spontaneous passage of stool, although with less cramping. The pt was discharged to hospice in a much more comfortable state. His underlying disease continued to progress and he died approximately three weeks later in hospice.

OIC is often a cause of great distress in pts with AI. SC MNTX has been shown to rapidly induce laxation in AI pts with OIC. This pt responded to MNTX despite the fact that he had spinal cord compression and was receiving high-dose opioids. SC MNTX may be useful in OIC in cases where there is also a neurologic component to the constipation.

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### A Rare Cause of Granulomatous Hepatitis Presenting as Fever of Unknown Origin

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**Case:** A 73 year old female with a past medical history of diabetes, presented with fatigue and fever. These symptoms began two months prior to admission and were noted after a femoral popliteal bypass two weeks prior to admission. Elevated liver enzymes evaluated by abdominal ultrasound revealed echogenic foci in the liver. These foci were consistent with hepatic abscesses, with ring enhancement and surrounding hyperemia on CT and MRI imaging. Liver biopsy performed on three separate occasions revealed necrotizing granulomatous inflammation, with histological features highly suggestive of an infectious etiology. AFB smear was negative, but tissue culture grew *Mycobacterium abscessus* one month later. After discharge, she again developed fever with enlarging abscesses on CT scan. She is currently doing well on imipenem, ceftriaxone, and amikacin.

**Investigation:** Our patient underwent extensive investigations that led to the diagnosis by culture of the liver biopsy. Initial workup for a fever of unknown origin, revealed WBC of 12.7, AST of 69, ALT of 56, alkaline phosphatase of 343, albumin of 3.7, an INR of 2.4. Blood cultures were negative on numerous occasions. Chest x-ray was clear. Tests for cryptosporidium, *E. histolytica*, *B. burgdorferi*, malaria, coccidiomycosis, histoplasmosis, brucella, tularemia, rocky mountain spotted fever and syphilis were all negative. Viral studies ruled out the hepatitises, CMV, EBV and HIV. The necrotizing granulomas found on core needle liver biopsy ruled out sarcoid and drug induced granuloma. Autoimmune etiologies such as Wegeners granulomatosis, PBC, PSC, and autoimmune liver disease were also ruled out.

**Discussion:** Hepatic granuloma is a immune reaction brought on by many etiologies. Often the causative agent remains unknown. In the United States, sarcoidosis and tuberculosis are the most common etiological factors causing hepatic granuloma. Liver biopsy from our patient grew *Mycobacterium abscessus*. This infectious agent has been documented in cases of soft tissue infections in post-surgical and traumatic skin wounds. It has also been isolated in patients with cystic fibrosis. After careful review of the literature, *M. abscessus* has never been reported to be responsible in the formation of liver

granulomata in humans. This case emphasizes consideration of other more obscure and rare etiologies such as a M. abscessus infection as a possible cause for granulomatous hepatitis and hepatic microabscess formation.

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### **Pneumatosis Cystoides Intestinalis in a Patient with Scleroderma and Idiopathic Pancreatic Exocrine Insufficiency**

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**Case Presentation:** A 43 year old female with limited systemic scleroderma and chronic diarrhea was admitted to our hospital with dehydration. At the time of admission the patient was having 10–15 small volume, watery bowel movements a day. She was afebrile and had no abdominal pain. She had previously been diagnosed with small bowel bacterial overgrowth but did not respond to a recent course of broad spectrum antibiotics. During her hospitalization, high stool output and fat soluble vitamin deficiency were noted. Pancreatic function testing was performed and showed pancreatic exocrine insufficiency. An abdominal CT scan was obtained to evaluate the pancreas and showed no structural pancreatic abnormalities. Incidentally, pneumoperitoneum with jejunal pneumatosis was noted. A diagnosis of pneumatosis cystoides intestinalis (PCI) was made. The patient was managed conservatively with pancreatic enzyme replacement alone. Stool frequency had decreased to 1–2 bowel movements per day at the time of discharge.

**Discussion:** PCI is a rare complication of systemic scleroderma. The clinical presentation is nonspecific and may involve nausea, diarrhea, constipation or abdominal pain. Abdominal tenderness on exam is variable. Radiographic findings typically include bowel wall cysts and pneumoperitoneum. Pneumoperitoneum is due to cyst rupture and is typically asymptomatic. Conservative management is recommended.

Systemic scleroderma is characterized by sclerosis of skin and visceral organs. It is divided into three categories: limited, diffuse, and sine scleroderma based on the extent of skin involvement. Previous reports of PCI in association with scleroderma have been in the setting of diffuse systemic scleroderma, with only one prior case report of PCI in limited systemic scleroderma.

Interestingly, our patient also had idiopathic pancreatic exocrine insufficiency and treatment with pancreatic enzymes resolved her diarrhea. To our knowledge, this is the first case report of these three diseases in the same patient. The combination of these diseases may represent polyautoimmunity in this patient.

**Conclusion:** PCI is a rare complication of limited systemic scleroderma, with one previous case described in the literature. We describe the first report of PCI with systemic scleroderma in association with idiopathic pancreatic exocrine insufficiency.

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### **Abernethy Malformation – A Rare Case and Method of Detection**

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Congenital absence of the portal vein (CAPV), or Abernethy malformation, is a rare malformation of the splanchnic venous system. CAPV has been associated with liver neoplasms, cardiac anomalies, and musculoskeletal abnormalities. In this case report, a patient with Abernethy malformation and a hepatic mass is described. The mass was visualized under EUS and underwent FNA which may represent the first Abernethy malformation visualized on EUS.

**Case:** 54 yo female with idiopathic cardiomyopathy s/p cardiac transplant who presented to an outside hospital with a 3-day progressive cognitive de-

cline. A head CT revealed an abnormality described as a mass or aneurysm. The patient was transferred to the University Hospital with confusion but otherwise stable. A head MRI showed an unruptured, 1 cm, right middle cerebral artery aneurysm. Serum chemistries, complete urine drug screen, UA and culture, blood cultures, chest x-ray, and lumbar puncture were obtained and only remarkable for an elevated alkaline phosphatase (306 U/L) and ammonia (74 mcmol/L). Viral hepatitis panel, AMA, and ANA were negative. An EEG showed diffuse bilateral slowing, consistent with encephalopathy. Lactulose therapy was initiated. An abdominal ultrasound revealed an absence of her portal vein and a 3.8 × 4.0 cm echogenic mass in the right lobe of her liver. An abdominal CT showed heterogeneous densities in the right and left lobes, possible cirrhosis, and no portal vein. A mesenteric angiogram showed the superior mesenteric vein and splenic vein flowing directly into the IVC with no portal vein. A CT-guided biopsy of the hepatic lesion showed periportal fibrosis with no malignancy or cirrhosis. The patient's mental status improved with lactulose. Follow-up of her hepatic lesions by ultrasound revealed no increase in size and serial alpha-feta proteins were normal. EUS was performed and showed gastric varices, absent portal vein, and a 1.5 cm left lobe hyperechoic lesion, which underwent FNA revealing only benign hepatocytes, ductal cells, and stromal cells. The patient continues to be monitored closely with no recurrent encephalopathy or increase in the hepatic mass.

**Conclusions:** This case demonstrates a rare finding of Abernethy malformation in an adult. Even more rare, this case utilized EUS with FNA to visualize the malformation and biopsy the hepatic mass. With the increasing use of EUS, more rare pathologies may be identified in the future, improving our diagnostic abilities.

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### **Systemic (AL) Amyloidosis Diagnosed on Duodenal Biopsies in a Patient Presenting with Mucosal Friability, Hepatomegaly and Weight Loss**

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**Case Report:** A 33 year-old African American male presented with a 2 week history of blood pooling in his posterior pharynx. He also described a 40 lb weight loss and increasing sharp right upper quadrant pain over the preceding 6 months. Physical exam revealed a chronically ill-appearing young man with marked nodular hepatomegaly and blood oozing from his oropharynx. Initial labs were remarkable for a mild normocytic anemia with hematocrit of 30.3, calcium of 11.7 mg/dl (8.9–10.3), albumin of 2.8 gm/dl (2.5–5), ast of 112 u/l (10–42), ggt of 111 u/l (7–64), alk phos of 585 (38–126) u/l, tbili of 2.1 mg/dl (0.3–1.6), and an inr of 1.6. The patient underwent upper endoscopy, which showed subtle granular duodenal mucosa and mild diffuse friability. Duodenal biopsies revealed extensive amyloidosis. Serum and urine protein electrophoresis showed monoclonal light chains. The clinical presentation was most consistent with systemic (AL) amyloidosis. The patient was started on a course of melphalan and dexamethasone and subsequently discharged home.

**Discussion:** Systemic (AL) amyloidosis is the most common and also the most lethal form of amyloidosis. It results from deposition of insoluble monoclonal immunoglobulin light chain fragments in various organs. The coexisting monoclonal gammopathy is usually low-grade and otherwise benign. Common clinical findings include weight loss, congestive heart failure, proteinuria, neuropathy and hepatomegaly. Despite the infrequency of GI symptoms, duodenum biopsies are clearly more sensitive than abdominal fat biopsies, which have a sensitivity of only 75%. Duodenal biopsies have higher yield than other parts of the GI tract, including rectal biopsies (98% compared to 86%). Characteristic endoscopic findings include multiple polypoid protrusions and fine granular mucosa, but mucosal friability, erosions and ulcerations are also seen. Our case demonstrates the importance of upper endoscopy and duodenal biopsies as primary diagnostic tools. In

patients presenting with friable mucosa, hepatomegaly and weight loss, amyloidosis should be considered. Our early endoscopic approach led to a swift diagnosis, which minimized the number of diagnostic tests and focused most of the patient's hospital stay on treatment.

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### Hemorrhagic Small Bowel Renal Cell Metastasis Diagnosed by Double Balloon Enteroscopy

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Recent advances in enteroscopy have made evaluation of the small bowel feasible. The utility of capsule endoscopy is solely diagnostic. Double balloon enteroscopy (DBE) permits examination of the entire small bowel and allows for diagnostic and therapeutic maneuvers. Through tattooing DBE provides a means for rapid laparoscopic localization of small bowel lesions.

**Case Report:** We report a case of a 65 year old woman transferred for melena without hemodynamic instability. Medical history was remarkable for hypertension, and left nephrectomy for renal cell carcinoma. Upper endoscopy and colonoscopy were negative. She was transfused three units and discharged with a hemoglobin of 10.6. Four days after discharge, labs revealed a hemoglobin of 7.2. On readmission, bleeding scan identified a source in the right upper quadrant small bowel region. Capsule endoscopy revealed a possible AVM, and ulcers in the ileum. The patient was transferred to our institution for DBE to specifically localize, identify, and treat the bleeding source.

The DBE system allowed deep insertion into the small bowel. A mass with a friable surface was identified on a broad stalk with ulcer at the base. Multiple small biopsies were obtained. India ink injections were placed 120 degrees apart, 3 cm proximal to the lesion. Biopsy results were consistent with metastatic renal cell carcinoma and the patient was taken to the OR for resection.

**Discussion:** The small bowel is an uncommon source of GI bleed. Approximately 5% of gastrointestinal bleeds cannot be localized after extensive workup including panendoscopy and capsule endoscopy. Of these, 27% are small bowel AVMs or tumors. Other small bowel bleeding lesions include gastrointestinal stromal tumors, carcinoids, and lymphomas.

At our center DBE is utilized in the evaluation of obscure-occult, and obscure-overt bleeding. We have found DBE to be safe and effective in diagnosing and treating many unusual lesions of the small bowel.

Renal cell metastasis to the small bowel are rare and scant reports of intussusception and bleeding secondary to these lesions can be found in the literature. Here we present the first case report of a small bowel renal cell metastasis diagnosed at DBE, which was subsequently removed laparoscopically. Tattooing of this endoluminal lesion permitted an expeditious and directed laparoscopic resection of the lesion.

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### Successful Late Treatment of Boerhaave's Syndrome with Esophageal Stenting

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We report two cases of Boerhaave's syndrome treated with esophageal stenting. The literature suggests early stenting to be advantageous. Historically, it was shown that after 24–48 hours, survival was enhanced with surgical repair of the esophagus to avoid fulminant mediastinitis. We report two successful cases treated with esophageal stenting beyond 48 hours.

Patient A is a 56 year old male presenting with emesis and abdominal pain of four days duration. Past history included COPD. Physical exam revealed subcutaneous emphysema and decreased breath sounds. CT scan revealed

pneumomediastinum, and left pleural effusion. Initial diagnosis of Boerhaave's was delayed until day 5 when he decompensated, had an increase in WBC and required BIPAP. The pleural effusion was drained. An endoscopy was performed revealing a 2 cm full thickness tear on the posterior-lateral wall of the esophagus. A Polyflex stent was placed, broad-spectrum antibiotics were initiated, and the patient was taken to the OR for mediastinal debridement. The patient was discharged one week later and returned in five weeks for endoscopic stent removal with complete healing of the esophagus. Patient B is a 78 year old female presenting with hematemesis and epigastric pain. Pain radiated to her back after 5 episodes of emesis. Her past medical history included COPD and GERD. Physical exam revealed coarse breath sounds in the left lung, and a soft diffusely tender abdomen. CT chest revealed pneumomediastinum with esophageal perforation and necrotizing pneumonitis in the left lower lobe. Endoscopy performed revealed an exudative scar with a 3 cm area of perforation. An Alimaxx esophageal stent was placed at 72 hours after presentation, broad-spectrum antibiotics were initiated, and the empyema was drained. The patient was discharged one week later in good health, and returned after six weeks for stent removal. Placement of self-expanding metal stents successfully beyond the area of perforation requires fluoroscopic or endoscopic guidance. Polyflex stents are favored over traditional metallic stents because they minimize granulation tissue formation, and tissue ingrowth, thus promoting minimal trauma to the esophageal wall during removal. The Alimaxx stent is covered, it causes minimal granulation tissue formation, and has a suture designed for repositioning and removal. Late endoscopic treatment of Boerhaave's syndrome with esophageal stenting is beneficial and should be considered first line therapy.

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### Acute Esophageal Necrosis: Two Cases of a Rare Endoscopic Finding

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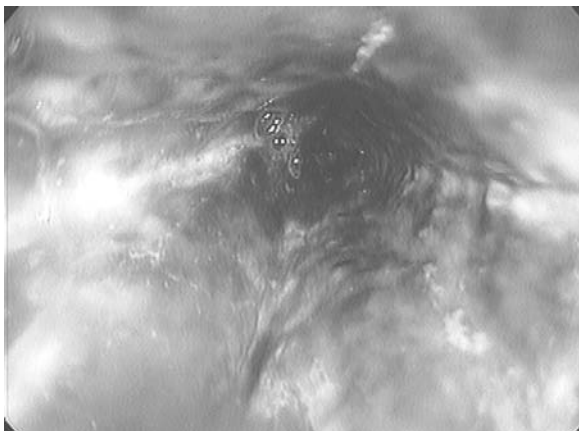
Acute esophageal necrosis (AEN) is a rare finding and is estimated to occur in 0.01% of all patients undergoing endoscopy. We aim to report two cases of AEN.

The first patient, a 79-year-old woman presented with coffee ground emesis. She was in atrial fibrillation with a rapid ventricular response. Her heart rate was controlled with diltiazem and an EGD was performed.

The second patient, a 50-year-old woman was admitted for evaluation of fever, weakness, and facial rash of two weeks duration. During her hospitalization, she developed acute renal failure and pancytopenia. A renal biopsy established the diagnosis of lupus nephritis. While in the hospital, she developed severe odynophagia and an EGD was performed.

In both patients, EGD demonstrated circumferential black esophageal mucosa with overlying white exudates and underlying pink granulation tissue (see figure). There was a sharp transition to normal appearing mucosa at the GE junction. Esophageal mucosal biopsies in the first patient revealed fragments of inflammatory and necrotic tissue. Because of her pancytopenia, biopsies were not obtained in the second patient. Both were started on IV PPI, sucralfate and were not allowed oral intake. Both patients had a repeat EGD that demonstrated resolving esophageal necrosis with confluent white plaques. Four months later, the first patient presented to the emergency department with a gangrenous right foot and expired two days later. Six months later, the second patient has not had a recurrence of her odynophagia.

AEN is a rare event the etiology of which is usually unknown. The diagnosis is usually made in the appropriate clinical setting with consistent endoscopic findings. The prognosis for patients who develop AEN is poor because 60% die with the disease or suffer complications like esophageal strictures. Most deaths in patients with AEN are due to an underlying medical condition rather than AEN itself. Because of its rarity there are no prospective studies of the management of AEN. Management of AEN could include no oral intake, treatment of the underlying illness, acid suppression, and sucralfate.[figure1]



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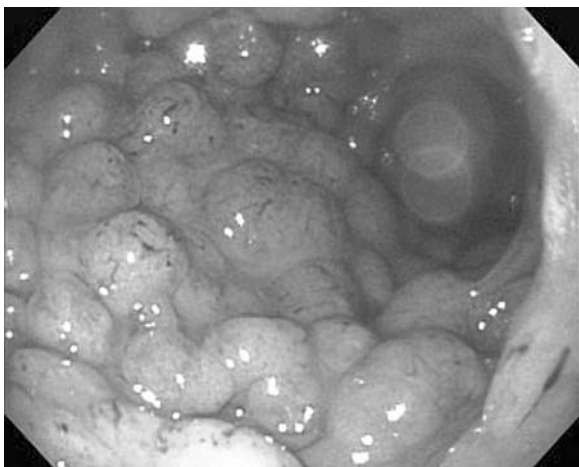
### Menetrier's Disease: Endoscopic Ultrasound Imaging To Support the Diagnosis

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A 57 year old man was evaluated for 6 months of loose, non-bloody stools, abdominal cramping and nausea. Leg swelling bilaterally was present for the prior 2 months as well. Stool studies were negative. Colonoscopy performed 4 months prior did not show any colitis or active inflammation, and albumin level measured 2.8 gms/dl (normal 3.5–4.5 gm/dl). CT scan of the abdomen showed diffuse thickening of the gastric wall. EGD displayed markedly enlarged gastric folds, some with a polypoid appearance in the proximal stomach (Fig. 1)/ Copious viscous mucous and a distinct transition to normal gastric mucosa near the antrum was observed. EUS (Fig 2) revealed the hypertrophy was relegated to the mucosa, measuring 14 mm. Biopsies showed foveolar hyperplasia, glandular cystic dilation with smooth muscle proliferation in the lamina propria. HEV staining for H. Pylori was negative. Findings consistent with Menetrier's disease.

Menetrier's disease is a rare, acquired, premalignant disorder of the stomach which occurs more often in men than women (3:1). The presentation is often insidious, with non specific complaints of abdominal pain, nausea, vomiting, diarrhea and peripheral edema.<sup>1</sup> Characteristics include hypertrophied gastric folds, excess mucous production, hypochlorhydria and hypoproteinemia. Etiology is unknown.

Gastric biopsies are needed for the diagnosis. Mainstays of therapy include H2 blockers and anticholinergics which are believed to decrease protein loss. As per the literature, roughly 15% have been associated with a carcinoma. A good portion of these patients go on to develop atrophic gastritis, some



will have a self limiting course and others will continue to suffer for years.<sup>1</sup> This patient was treated with an H2 blocker and a high protein diet and has done well.

**Ref:** 1. Scharschmidt, BF. The natural history of hypertrophic gastropathy. *Am J Med* 1977;63:644.[figure1][figure2]



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### Early Detection of Diaphragm's Disease of the Small Bowel and Impact on Management

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Since the term 'diaphragm's disease' was first used in 1988, our knowledge of the disease has expanded.

We are reporting on a patient who presented with intermittent incomplete small bowel obstruction. He was diagnosed with multiple small bowel strictures on M2A consistent with NSAID induced diaphragm's disease.

This is a 47 year old male who presented with abdominal pain, nausea and vomiting. His pain was dull in nature and periumbilical in location. There were no obvious exacerbating or relieving factors.

His PMHx: hypertension, juvenile rheumatoid arthritis and multiple joints replacements.

Medications: Norvasc, Maxzide, Naprosyn, Darvocet, Lortab, and Ambien. On physical exam he has multiple joint deformities consistent with Juvenile RA. His Abdomen was distended, tender, with hyperactive bowel sound. He had normal labs.

Abdominal and pelvic CT showed multiple dilated fluid filled loops of small bowel without an obvious transition zone or wall thickening.

His small bowel follow through showed some dilated loop of bowel in the ileum. During this admission he was treated with NGT decompression and his symptoms improved without surgical intervention.

He represented again a few weeks later with similar symptoms. His CT and small bowel follow through were identical to those of the prior admission. He was treated in a similar manner as previously; but once symptoms resolved, we performed an M2A study. The study showed multiple strictures throughout the small bowel. The capsule was trapped in one of these strictures for a short period of time, but did pass through without any complications.

The patient was advised to stop all NSAID's and was started on (Miralax) 2 for constipation. The patient has been followed for two years, on a regular basis, and has not required any further hospitalization or treatment for his GI tract.

This is a unique case because of the early detection of small bowel diaphragm's disease along with the cessation of NSAID's saved this debilitated patient from potential small bowel obstruction and the need for surgical intervention.[figure1]



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#### Colonic Co-Infection of Histoplasma and CMV in a HIV/AIDS Patient Mimicking Carcinoma

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A 45 year old male with known history of hemophilia and HIV/AIDS presented with right upper quadrant pain for three weeks, associated with

weight loss and fever. He had declined anti-viral therapy. Physical exam revealed tenderness in the right upper quadrant without rebound and normal bowel sounds. Laboratory tests included: WBC: 2000, hemoglobin: 11.1, AST: 61, ALT: 46, albumin: 3.7, CD4 count: 17, HCV antibody was positive. CT scan revealed an apple core lesion at cecum suggestive of carcinoma (Fig. 1A&B). Colonoscopy revealed a mass in the proximal ascending colon, just distal to the cecum (Fig. 1C). There were also ulcers in the cecum, ascending, and transverse colon. Biopsy of the mass showed histoplasmosis and CMV co-infection (Fig. 1D&E). Antimicrobial therapy was initiated.

In immunocompromised patients, colonic histoplasmosis is well known to cause mass like lesion, mimicking carcinoma. CMV often causes ulcers in the colon, but CMV associated mass lesion of the colon has also been reported in several cases; the finding of both organisms in a mass lesion in the colon is rare.[figure1]

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#### A Case of Obscure Gastrointestinal Bleeding

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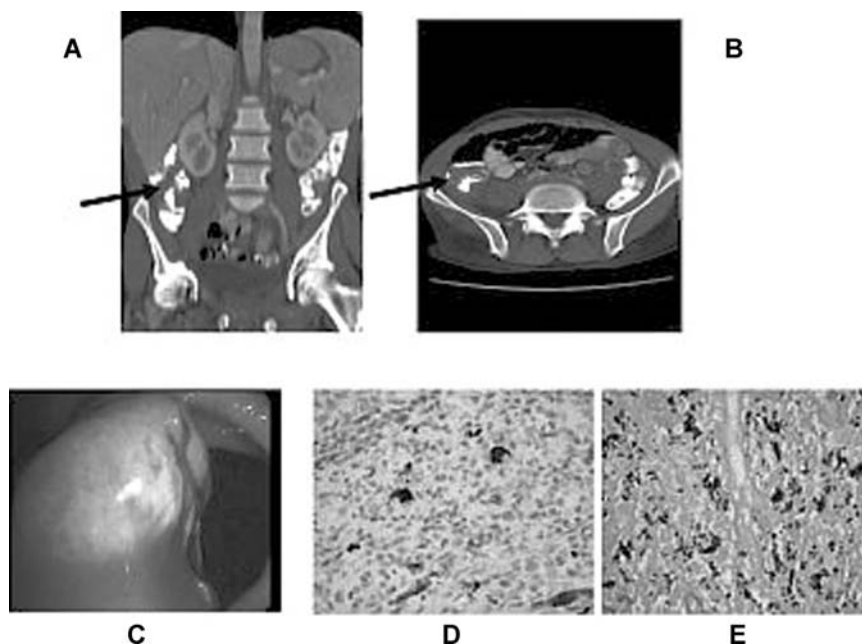
A 20 yo M with no PMH presented to an outside hospital with dark stools and decreased exercise tolerance. His hemoglobin (Hb) was 7.8 g/dL. EGD, Colonoscopy, Meckel's Scan and Small Bowel Series were all unremarkable; the patient was stable during workup and was discharged. Two months later, he syncopized due to recurrent bleeding. His Hb level was 7.5 g/dL with MCV of 68. Workup including enteroscopy, Technetium-labeled RBC scan, and CT scan were unremarkable. Colonoscopy revealed blood throughout the colon; he was transferred to our ICU.

Initial evaluation included a normal Meckel's Scan and RBC scan.

Patient was given a heparin challenge while in the ICU. On heparin, the patient rebled, but was hemodynamically stable. A repeat bleeding scan was positive for activity in the ileum or right colon. Colonoscopy revealed blood throughout the colon but not in the terminal ileum.

Video capsule endoscopy was performed while the patient remained on heparin.

Distal small bowel images revealed a diverticular orifice with surrounding blood. [figure1]Exploratory laparoscopy revealed a Meckel's Diverticulum.[figure2] A diverticulectomy was performed and the specimen revealed



atopic gastric mucosa within the diverticulum. The patient made an uneventful recovery.



1. Capsule endoscopy is an effective method to diagnose Meckel's Diverticulum.
2. A heparin challenge in a monitored setting can aid in the localization of obscure bleeding source.
3. Meckel's Scan has an approximately 60% sensitivity in the diagnosis of Meckel's Diverticulum in the adult population<sup>a</sup>; capsule endoscopy and exploratory laparoscopy should be pursued when clinical suspicion for Meckel's remains high.
4. Lin S, et al. Gastrointestinal bleeding in adult patients with Meckel's diverticulum: the role of technetium 99m pertechnetate scan. *South Med J* 2002;95(11):1338–41.

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#### UGI Bleeding Secondary to Pseudoxanthoma Elasticum

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A 39 year old Pakistani man with diabetes, hypertension and a prior CVA presented to the emergency department with abdominal pain and melena.

The patient had two prior gastrointestinal (GI) bleeding, occurring 6 and 9 years earlier. Each of those events required massive transfusions, the first requiring 17 units of packed red blood cells (RBCs) and the second 25 units of packed RBCs. During the previous hospitalizations for GI bleeding, he was diagnosed with pseudoxanthoma elasticum (PXE) based on a biopsy of a skin nodule in the neck. After admission, the patient underwent four esophagogastroduodenoscopies (EGDs) for melena. The initial EGD revealed diffuse blood oozing from multiple petechiae and linear erosions in the stomach, for which argon plasma coagulation was applied without success. He underwent additional two EGDs, one colonoscopy and a bleeding scan that were all unrevealing. The final EGD showed three ulcers with a pigmented protuberance in the antrum; hemoclips, epinephrine injection and BiCAP electrocautery were applied with a short term hemostasis. Despite these attempts, he continued to have melena and underwent a total gastrectomy and Roux-en-Y esophagojejunostomy. The gastrectomy specimen showed a Dieulafoy's ulcer in the proximal body that was noted in a background of vascular abnormalities, including fibro-intimal thickening and sclerosis with fragmentation and calcification of the internal elastic lamina, consistent with PXE. After surgery, the patient was discharged home without evidence of recurrent bleeding and remains stable. PXE is an autosomal recessive, multisystem disorder that affects primarily the skin, eyes and vascular system. GI bleeding, usually recurrent and of gastric origin, has been reported in 13% of affected patients. GI bleeding is thought to result from degeneration of elastic fibers in the arterial wall, which leads to aneurysmal dilatation and subsequent rupture of the vessels. There have been two prior published case reports that associated Dieulafoy's ulcer with upper GI bleeding in PXE. In our case given the pathologic findings of Dieulafoy's lesion and continued bleeding despite multiple endoscopic therapies we postulate that the Dieulafoy's ulcer was a likely cause of the bleeding. As in our case, total gastrectomy may be a justifiable alternative when medical treatment is ineffective. However, we believe that in a subset of patients with PXE and continued GI bleeding all attempts to rule out a Dieulafoy's ulcer should be made prior to undergoing definitive surgery.

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#### Cytomegalovirus Infection Associated with Esophagitis and Esophageal Stricture after Liver Transplantation

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Cytomegalovirus (CMV) esophagitis is a rare entity most often associated with AIDS and bone marrow transplantation. We report a case of a liver transplant recipient with severe CMV esophagitis that rapidly progressed to esophageal obstruction.

A 46-year-old woman with primary biliary cirrhosis underwent a cadaveric liver transplantation. The patient was CMV – and received a CMV + graft. Tacrolimus 2 mg twice daily, mycophenolate mofetil (MMF) 750 mg twice daily, and valganciclovir 450 mg every other day was initiated. The patient presented 6 months after transplantation with abdominal pain and dysphagia. An EGD revealed circumferential distal esophageal ulceration that extended for 3 cm. Esophageal biopsies, viral cultures, fungal cultures, herpes virus antibodies, CMV DNA and CMV antigen testing were unremarkable. The patient was placed on a liquid diet with PPIs and carafate slurry. One week later, an EGD was performed for new onset odynophagia. Persistent circumferential distal esophageal ulcerations were noted. The esophageal brushings EGD revealed positive rapid cultures for CMV. MMF was discontinued and IV ganciclovir was instituted. The patient required IV fluid support and was unable to take oral medications. An EGD performed two weeks later revealed a tight esophageal stricture with an intraluminal diameter of less than 5 mm and a length of 4 cm that could not be traversed with a Pentax 2731 videoendoscope. The stricture was dilated using serial balloon dilations using a Bard Eliminator through the scope type dilator. Esophageal biopsies 2 months after the initial presentation revealed no evidence of persistent

CMV infection. Esophageal dilations were necessary at 10-day intervals for 6 sessions until the patient was able to resume a regular diet. Valganciclovir was continued.

Risk factors for CMV esophagitis included CMV – recipient status, receipt of a CMV + graft, leukopenia, discontinuation of CMV prophylaxis, and immunosuppression. Initial serologic and biopsy examinations were unrevealing. However CMV infection was confirmed with a positive biopsy culture. This is the first case of CMV esophagitis complicated by rapid esophageal stricture formation in a liver transplant patient. It would seem prudent to maintain CMV prophylaxis in liver transplant recipients with multiple risk factors.

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### Thumbs Up: Endoscopist's Thumb as an Occupational Hazard Related to High Volume Endoscopy

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Endoscopists performing high volume endoscopies are at risk of developing occupational injury related to mechanical stress on the tendons at the base of the thumb. de Quervains's syndrome, or stenosing tenosynovitis of the thumb tendon, has been reported as an occupational hazard of endoscopy [1]. It occurs as a result of repetitive overuse of the left thumb while grasping and turning the wheels of the endoscope while moving the wrist in radial and ulnar directions. This leads to thickening, inflammation and eventually stenosis of the fibrous tendon sheath as it passes over the distal radius. The friction-induced tenosynovitis can lead to fibrosis and eventually stenosing tenosynovitis. We describe a case of de Quervains's syndrome of the left thumb occurring in a high volume endoscopist that responded to conservative therapy.

A 50-yr-old right-handed clinical gastroenterologist who had performed more than 25,000 endoscopies over the prior twenty years, with an increase in procedural volume in the last six years, complained of severe pain at the base of his left thumb. Pain would occur with exaggerated thumb movements during endoscopy. This interfered with performance of endoscopy. The pain would also awaken the physician in the middle of the night and interrupt sleep. Examination revealed moderate swelling and point tenderness over the left thumb tendons at the distal portion of the radial styloid. A positive Finkelstein's test was demonstrated, consistent with de Quervains's syndrome. He was treated with aspirin, thumb rest for one week, and a thumb splint at night. This treatment regimen resulted in clinical improvement such as to be able to continue his regular endoscopy schedule. de Quervains's tenosynovitis affecting the tendons of the thumb can occur as an occupational hazard of high volume endoscopy (1). It is caused by repetitive overuse of the left thumb during grasping and turning of the wheels of the endoscope while moving the wrist in radial and ulnar directions. The syndrome can respond to conservative therapy, as in our case. Other therapies include steroid injection with a reported 90% response rate, and surgical incision of the tendon. Rarely, when this syndrome is advanced, it may terminate an endoscopic career. (1) Cappell MS. Colonoscopist's thumb: DeQuervain's syndrome (tenosynovitis of the left thumb) associated with overuse during endoscopy. *Gastrointestinal Endoscopy* 2006, 64:841–843.

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### Interferon-Alpha Induced Thyroid Disease in Patients Being Treated for Hepatitis C

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**Introduction:** Interferon (IFN)-alpha is indicated for a variety of malignancies and chronic viral illnesses and is associated with an increase in autoimmune thyroid disease. IFN-alpha is critical in viral Hepatitis C (HCV) treatment. Clinically significant thyroid disease induced by IFN-alpha may

result in discontinuing a therapeutic agent shown to improve survival and decrease morbidity in HCV infected patients. We present two cases to show the different clinical presentations of thyroid disease secondary to IFN therapy for HCV treatment and discuss strategies for diagnosis and management.

**Case presentations:** Case #1: 48 year-old man with a family history of hypothyroidism was admitted with abdominal pain and coffee-ground emesis. Six months after initiating therapy with IFN-alpha and ribavirin for HCV he noted a 50-lb weight loss with fine tremors and palpitations, which he attributed to anxiety. Thyroid stimulating hormone (TSH) was normal prior to therapy. Physical examination revealed a thin, slightly anxious male with fine, resting tremors. The thyroid gland was not enlarged and no masses, nodules, tenderness, or bruits were noted. Lab work revealed the TSH was 0.03 (normal 0.4–4.7 uIU/mL) and free thyroxine (FT4) was 3.4 (normal 0.58–1.64 ng/dL). Thyroid stimulating immunoglobulin was 2.5 (normal <1.3) and thyroid peroxidase antibody was <20 (normal is <40 IU/mL). A 123-iodine thyroid uptake and scan showed diffuse homogenous uptake of 17.8% at 4 hours (upper limit of normal is 15%).

Case #2: 48 year-old woman with a family history of hypothyroidism treated with IFN-alpha and ribavirin for HCV. Before initiating IFN therapy, her TSH was 4.35 uIU/mL. After 7 months of therapy, patient stated her rings were getting tight and she was "retaining water". A repeat TSH level was 321.38 uIU/mL and FT4 was <0.50 ng/dL. Thyroid hormone replacement was started and her symptoms resolved.

**Discussion:** Thyroid disease is a frequent complication of IFN therapy with variable expressions and different long-term outcomes. Early symptoms of thyroid disease may be wrongly attributed to HCV symptoms and IFN side effects leading to a delay in diagnosis and discontinuation of IFN-alpha. The exact mechanism by which IFN induces thyroid autoimmunity is unknown, but given the high prevalence of this complication physicians need to be aware of the spectrum of clinical presentations, etiology, and management.

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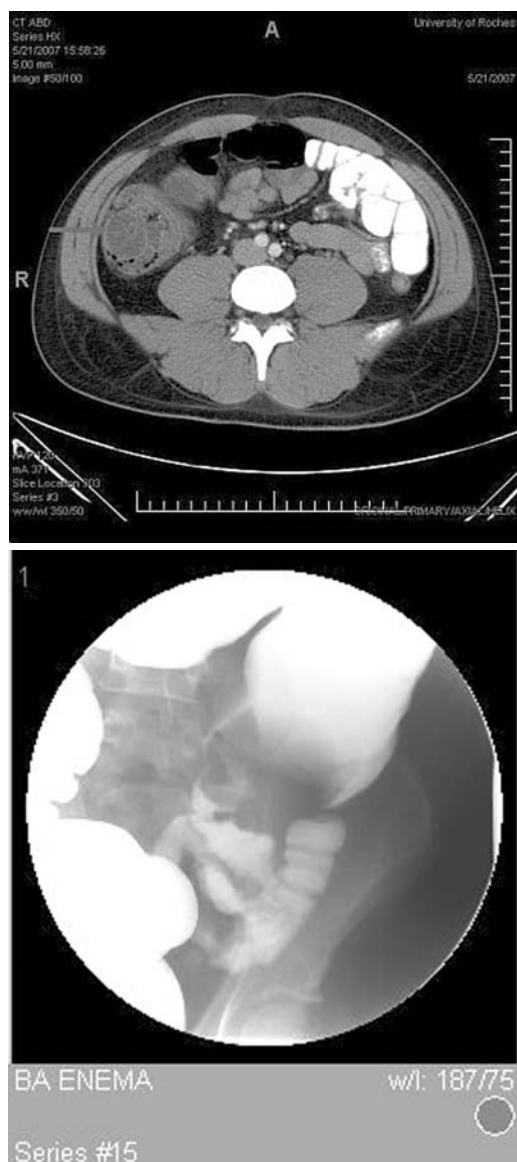
### A Rare Case of Intussusception in a Patient with Typhlitis Managed Successfully by Barium Enema Reduction

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Intussusception in adults is an uncommon entity associated with an underlying pathologic cause in 70–90% of cases. Surgical resection is the treatment of choice as up to 50% of adult intussusception are caused by malignancy. Here we describe a case of a successful reduction of an intussusception with barium enema in a patient with neutropenic colitis.

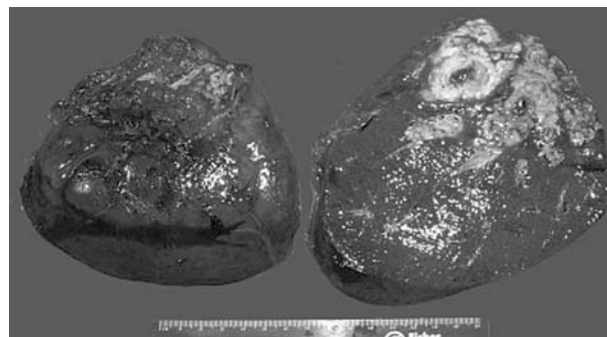
A 26 year-old Caucasian male was admitted to Strong Memorial Hospital for treatment of acute lymphocytic leukemia, and underwent induction chemotherapy with daunorubicin, vincristine, and prednisone. He did well until hospital day #15 when he began experiencing right lower quadrant abdominal pain. A subsequent CT scan revealed an ileocolic intussusception with pericecal fat stranding. [figure1] Because of his profound neutropenia and thrombocytopenia, he was initially treated conservatively with IV antibiotics. However, a repeat CT scan the following day showed a persistent intussusception with increasing dilation of small bowel loops. A barium enema was then performed which identified the intussusception at the hepatic flexure. With administration of additional pressure, contrast advanced proximally within the colon and entered the small bowel, despite a persistent filling defect in the cecum.[figure2] The concern for a residual intussusception prompted an exploratory laparoscopy which revealed normal anatomy of the ileocolic region. The appendix and cecum were hyperemic with evidence of neutropenic colitis. The patient did well postoperatively and was discharged fifteen days later.

To our knowledge, only two cases of intussusception in the setting of neutropenic colitis have been reported in the literature. Although more commonly used in children, barium enema resulted in the successful reduction of this abnormality as confirmed by diagnostic laparoscopy.



logic testing for chronic liver disease was negative. A CT scan revealed a 10.4 × 6.8 cm heterogeneous mass in the right lobe with multiple areas of necrosis and pneumobilia suggestive of a necrotic tumor. The patient was taken for a right hepatectomy and an 8 × 7.5 cm cystic yellow-tan hepatic mass was found (Figure). Histology showed multiple microabscesses surrounded by reactive and xanthomatous histiocytes (CD68+, S100-) with hemorrhage and focal cholangitis consistent with IPT. No malignant cells, viral inclusions, or parasites were seen and special stains for fungi and AFB were negative. The patient was discharged 9 days after the hepatectomy and has been doing well more than 6 months later.

IPT should be considered when patients present with clinical and radiological features mimicking malignant neoplasm. IPT is often mistaken radiologically for hepatocellular carcinoma, cholangiocarcinoma, or metastatic tumor. Directed biopsy may nondiagnostic. The diagnosis can often only be made after complete surgical resection. Hence, surgical resection is definitive for both diagnosis and treatment.[figure1]



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#### Inflammatory Pseudotumor of the Liver Mimicking Malignancy

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Inflammatory pseudotumor (IPT) of the liver is a rare inflammatory process often mistaken for hepatic malignancy. We report a case of a patient with IPT who presented with fever, mental status changes, and a hepatic mass who was successfully treated with a right hepatectomy.

A 67 year old Asian female presented with 2 weeks of fever and confusion. Laboratory evaluation revealed alkaline phosphatase 233 U/L, total bilirubin 2.2 mg/dL, AST 80 U/L, ALT 113 U/L, WBC  $17 \times 10^9$  cells/L. An MRI revealed an 8.6 × 6.2 cm cystic mass in the right lobe of the liver. A mammogram, EGD, and colonoscopy were unremarkable. FNA of the mass revealed acute inflammatory cells and benign hepatocytes. The patient was transferred to our hospital on empiric antibiotics. Laboratory evaluation revealed albumin 2.3 g/dL, alkaline phosphatase 501 U/L, total bilirubin 0.8 mg/dL, AST 39 U/L, ALT 23 U/L, AFP 2.8 ng/mL, CEA 2.8 ng/mL. Sero-

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#### Intestinal Tuberculosis Masquerading as Crohn's Disease

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A 30 year old man, presented to another hospital with 2 years of cramping abdominal pains which had markedly worsened over the last 3 months. The pain was associated with watery diarrhea and 30 pound weight loss. Of note, he immigrated to the U.S. from Nepal 4 years ago. His father had been treated for pulmonary tuberculosis (TB) 8 years ago. On admission, he was found to be markedly wasted with diffuse abdominal tenderness. CT showed extensive thickening of the right colon, with mild thickening of the transverse and descending colon. Small bowel series showed minimal irregularities of the terminal ileum. Colonoscopy at the other hospital was aborted at the transverse colon due to severe luminal narrowing by edema and inflammation. There were patchy areas of deep circumferential ulcerations, pseudopolyps, and erythema from the distal transverse colon to the rectosigmoid area. Biopsies revealed active inflammation with non-caseating granuloma and negative AFB staining. Chest X-Ray and PPD skin test were negative, as were HIV serology and stool studies. He was treated for Crohn's disease with oral mesalamine, intravenous methylprednisolone and intravenous ciprofloxacin and metronidazole. His diarrhea improved somewhat, but the abdominal pain did not. He continued to lose weight and required parenteral nutrition. He was ultimately transferred to our institution for further care. Repeat colonoscopy revealed deep ulcerations in the descending colon and visualized parts of the transverse colon. Infliximab was considered, but because of the patient's worsening clinical condition, he was referred for surgery. The surgical specimen ultimately revealed AFB-positive caseating granulomas. After several months of anti-TB therapy, he underwent reversal of ileostomy. TB is no longer considered a rare disease in the United States due to influx of immigrants from endemic areas, and from the growing AIDS population. The signs and symptoms of intestinal TB are often non-specific and a high index of suspicion must be maintained



to ensure a timely diagnosis. Diagnosis requires colonoscopy with multiple biopsies. Colonoscopic findings which favor intestinal TB include a patulous ileocecal valve in the setting of circumferential ulcers (rather than the often linear ulcers of Crohn's disease), scars, and pseudopolyps. If intestinal TB is suspected, empiric treatment may be warranted despite negative histology or culture results.

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### Hepatic Artery Pseudoaneurysm: A Unique Cause of Obscure Upper GI Bleeding

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Hepatic Artery Pseudoaneurysm (HAP) is a rare clinical entity and is usually associated with iatrogenic or traumatic etiologies, and almost always manifests with hemobilia. We report the first documented case of HAP in a patient with chronic cholecystitis without any underlying history of trauma or surgery, presenting as massive upper gastrointestinal hemorrhage (UGIH) without hemobilia.

A 73 year old Caucasian female with past history of NIDDM, hypertension, hyperlipidemia presented to ER with non-radiating epigastric pain, nausea and black melanonic stools for past 24 hours. Pertinent labs on admission showed a Hb of 10.3 g, WBC 12.3, T.B 2.3 mg, AST 525 U, ALT 451 U, ALP 133 U, BUN 35 and S.Cr 1.0. Abdominal ultrasound showed multiple gallstones, and the CT scan showed a large intraluminal echogenic structure consistent with a gallstone, with thickened GB wall. Over the next day, the patients Hb dropped to 6 g and upper GI Endoscopy (UGIE) revealed acute hemorrhage, possibility of a duodenal ulcer was entertained. To investigate the possibility of GB malignancy in view of the above radiological findings and CA 19-9 level of 2801, an ERCP was done which showed no hemobilia or stone, and a CBD stent was placed for patency. Patient continued to have UGIH with falling Hb, and multiple endoscopies failed to achieve adequate hemostasis. Subsequent UGIE study showed an adherent clot on the lateral wall with active oozing. Patient was then taken for selective catheterization and angiogram of the celiac trunk and right hepatic arteries, which yielded visualization of large extravasations of contrast from the inferior aspect of the right common hepatic artery and confirmed a pseudoaneurysm, eroding into the duodenal mucosa. Successful embolization and hemostasis was achieved. The patient also had a gall bladder biopsy to rule out malignancy, which revealed chronic active cholecystitis.

This case illustrates a extremely rare association of HAP with chronic cholecystitis presenting as UGIH in an unusual form and not as the classical hemobilia. Of the multiple case reports and series submitted for HAP, almost all have shown a preceding interventional procedure involving the hepatobiliary and pancreatic systems or history of trauma. HAP due to biliary inflammation is usually attributed to stone eroding into the artery or due to local weakness of vessel wall. Awareness of this rare presentation and association of HAP may allow early diagnosis and timely intervention.

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### Unusual Presentation of Acute Abdominal Pain in Polycystic Liver Disease Patient

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62 y/o man with history of chronic kidney disease Stage V on hemodialysis (HD) for 22 yrs secondary to polycystic kidney/liver disease with chronic abdominal pain. He underwent an endoscopic retrograde cholangiopancreatography (ERCP) twice for evaluation of a dilated common bile duct (CBD) and chronic pancreatitis identified on computed tomography (CT), most recently revealing grossly dilated CBD and perianipillary diverticulum. Patient developed acutely more severe abdominal pain 1 month after ERCP

during HD and was admitted to the hospital. Patient was found to have a temperature of 102° F, diffuse to RUQ tenderness, and delirium with white blood cell count (WBC) of  $5.1 \times 10^3/\text{cmm}$ , bands of 33%, total bilirubin 1.2 mg/dL, alkaline phosphatase 277 IU/L, aspartate aminotransferase 150 IU/L and alanine aminotransferase 132 IU/L. Surgical evaluation did not indicate an acute abdomen. Noncontrasted CT revealed interval enlargement of all cysts in the liver with debris, an enormous gallbladder, polycystic kidneys and diffuse atherosclerotic disease. Subsequently, patient's abdominal pain and mental status improved over the next two days with renal-doses of empiric antibiotics of levofloxacin, metronidazole, and gentamicin. On day 3, patient developed severe episode of abdominal pain and became distended with tympany/hypoactive bowel sounds. Plain radiograph of abdomen was consistent with small bowel obstruction/ileus. WBC rose to 18.0, temperature was 97.3° F, potassium 5.7 mmol/L, plasma bicarbonate 16 mEq/L. These changes prompted emergency abdominal laparotomy. Intraoperative exam revealed ruptured hepatic cyst and brown fluid freely floating in the abdominal cavity. Culture of fluid revealed *Escherichia coli* and *Enterococcus avium*. Drainage and washout of hepatic cyst completed at time of laparotomy. Patient subsequently declined clinically, required pressors and later expired, 2 days following surgical laparotomy.

**Discussion:** This case represents report of a ruptured infected hepatic cyst in a patient with polycystic kidney/liver disease presenting with nondistinct presentation initially, followed by acute cholangitis picture and later suggestion of small bowel obstruction/ischemic bowel presentation with acute abdomen in a chronically ill patient. Etiology of nidus for infectious process in hepatic cysts undetermined at this time, but possibly due to (chronic) cholecystitis. Hepatic cysts may rupture, but multiple cysts simultaneously causing morbidity is rare.

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### Cystic Duct Remnant as a Cause of Post-Cholecystectomy Syndrome Diagnosed by Endoscopic Ultrasound

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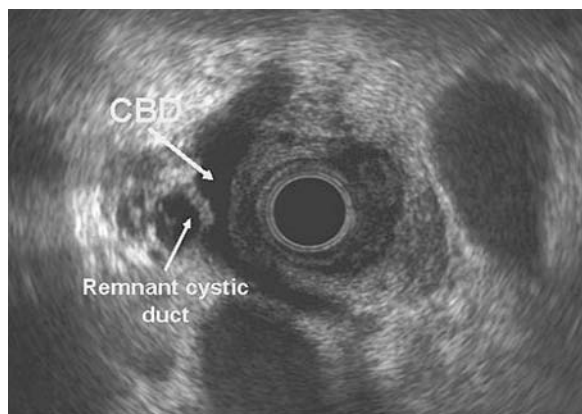
**Background:** Post-cholecystectomy syndrome can be the result of a cystic duct remnant. These patients may present with symptoms of cholecystitis in the setting of an absent gallbladder. The pathophysiology of this condition may be the result of sludge, stones, or debris in the remnant cystic duct. Its incidence has been correlated to the length of the remnant cystic duct.

**Case:** An 86 year-old man status post-cholecystectomy seven years prior secondary to gallstone pancreatitis presented with several episodes of right-sided chest discomfort. He had fever, abnormal liver chemistry and leukocytosis. Blood cultures grew gram negative rods. He was placed on intravenous antibiotics and underwent endoscopic ultrasound (EUS) to evaluate his biliary tree. This demonstrated a common bile duct of 7-mm. In the proximal portion of the CBD, there was an outpocket representing a cystic duct remnant with echogenic debris (Fig. 1). An endoscopic retrograde cholangiogram (ERC) was then performed. This revealed a cystic stump greater than 1 cm in length which contained a small stone. The stone was removed and a sphincterotomy was performed. The patient's clinical symptoms and laboratory abnormalities resolved. Four weeks later, the patient reported no further episodes of pain.

**Discussion:** Post-cholecystectomy syndrome may be the sequela of a remnant cystic duct. The incidence is unknown although it is thought to be more common in the age of laparoscopic cholecystectomy. When suspected, MRCP is the diagnostic test of choice. In our case, EUS suggested the disease which was confirmed and treated by ERC. In patients presenting with post-cholecystectomy syndrome it is important to consider cystic duct remnant in the differential diagnosis.

**Sources:** Zhou PH, Liu FL, Yao LQ, Qin XY. *Endoscopic diagnosis and treatment of post-cholecystectomy syndrome*. Hepatobiliary & Pancreatic Diseases International 2003; 2(1): 117-120.

Shaw C, O'Hanlon DM, Fenlon HM, McEntee GP. Cystic duct remnant and the 'Post-cholecystectomy Syndrome.' *Hepato-Gastroenterology* 2004; 51: 36–38.[figure1]



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#### Failed Use of Adalimumab in Maintaining Remission in Crohn's Disease during Pregnancy

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**Background:** Active Inflammatory Bowel Disease (IBD) during pregnancy is a risk factor for low birth weight, poor fetal outcome and premature delivery. Maintaining remission is critical, and medications targeting TNF- $\alpha$ , such as adalimumab, are most effective in treating Crohn's disease (CD). However, their safety and efficacy during pregnancy are not fully known. We report the failed use of adalimumab in maintaining remission during pregnancy in CD.

**Case:** RL is a 21-year-old woman who was diagnosed with IBD at age 17 when she experienced bloody diarrhea and weight loss following a miscarriage. She developed toxic megacolon necessitating a total proctocolectomy with ileal pouch anal anastomosis. An anal fistula which progressed into an abscess ensued. Pouchoscopy showed an ulcerated inflow tract that more resembled CD than UC. RL was started on infliximab, 6MP and Prednisone without significant improvement. Infliximab was subsequently discontinued. Repeated pouchoscopy showed ulceration at the ileoanal anastomosis site and adalimumab was added. At age 20, RL was in remission and became pregnant while taking adalimumab and 6MP. She presented with a tender right groin lymph node 6 months later. The node developed into a nonhealing perianal abscess and was thought to be a pouch-vaginal fistula secondary to CD. Drainage of the abscess was recommended but she elected to have it deferred until delivery. Fetal development was normal and she had a C-section at 36 weeks.

**Discussion:** Adalimumab's use in active CD during pregnancy has been described in several case reports, demonstrating success in attaining remission and preventing complications such as fistulas, strictures or abscesses. However, there have been no reports describing adalimumab's inability to control complications of CD during pregnancy. While adalimumab is rated pregnancy class B, crosses the placenta and has been identified in breast milk, it has not been shown to cause any adverse fetal events. Its efficacy remains unclear, as our patient manifested new fistulizing disease. A comparative registry evaluating the efficacy and toxicity of anti-TNF- $\alpha$  drugs is warranted. At this time, certolizumab, a pegylated anti-TNF- $\alpha$  drug, may be a good alternative during pregnancy, as it does not cross the placenta.

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#### Rectal Perforation Caused by a Holistic Colonic Cleansing

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**Introduction:** Colonic cleansing, also termed high water enema, colonic lavage or irrigation, is common in alternative medicine. It involves introduction of up to 50 liters of fluid into the colon through a rectal tube. It is believed to have a detoxifying effect. Risks include electrolyte imbalances, bowel perforation, and transmission of disease. We present a case of rectal perforation after colonic irrigation.

**Case:** 44-year-old African American lady presented with rectal pain. She had colonic irrigation at a holistic health center during the previous week. During irrigation, she felt sharp, severe rectal pain which steadily increased. She also noted small, loose stools, nausea, vomiting, and hematochezia. Temperature was 101°F; pulse 114 bpm. She had an obese, soft and non-tender abdomen, with bowel sounds present, but no organomegaly, guarding, or rebound tenderness. Rectal examination revealed no mass, normal anal sphincter tone, and hemoccult negative stool. Physical examination was otherwise normal. Initial pelvic CT imaging revealed extensive edema and extraluminal air around the rectum, suggesting a contained perforation, but no abscess. There was no free intra-abdominal air or ascites. Repeat CT scan at 1 week revealed a horseshoe shaped abscess at the anterior rectum, with oral contrast visible in the perirectal space. A defect in the anterior rectal wall was consistent with persistent rectal tear. The patient was managed nonsurgically with IV antibiotics and clinically improved. The patient underwent a gastrografin enema at 2 weeks but there was no further leak. The patient was discharged home on oral antibiotics.

**Discussion:** Colonic irrigation is a holistic procedure based on the concept of "autointoxication". Cases of bowel perforation are rarely reported; 3 cases of rectal perforation in Australia required surgery; 1 case in Singapore resulted in perineal gangrene. Diagnosis of rectal perforation is made by history, abdominal x-ray or CT scan. Clinical suspicion demands a careful history. In this case we treated the patient with intravenous antibiotics and no surgery was required. Surgical treatment may involve a colostomy, which has major risks and impact on a patient's life. Patients may not be aware of the possible risks; physicians should provide information to patients who participate in holistic medicine.

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#### Life-Threatening Hepatic Failure Associated with Entecavir Resistance Mutations I269I/T and T184L Two Years after Discontinuation of Lamivudine

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While entecavir (ETV) resistance is rare in nucleoside naïve HBV patients, it is more common in the presence of lamivudine resistance (LVD<sub>r</sub>) mutations. Despite this, ETV is reported to be effective in lamivudine-refractory patients.

We describe a 47 year old man with history of LVD<sub>r</sub> who presented with hepatic failure after being switched from adefovir (ADV) to entecavir (ETV). The patient initially presented in 1998 as a 38 year old man with chronic HBeAg positive HBV and cirrhosis and was started on lamivudine (LVD). In 2003, his ALT became elevated, and LVD was stopped and ADV started. Due to viremia and increasing creatinine, ADV was stopped and ETV started in 2005. His HBV DNA decreased to a nadir of 800 IU/mL in 2006. In February 2007, he developed virologic rebound with HVB DNA >38,000 IU/mL, and ADV was added. HBV genotypic analysis showed M204V, L180M, I169I/T, and T184L mutations, as well as a basal core promoter mutation G1764A. In March 2007, ADV was stopped and tenofovir added, followed by a

ten-fold decrease in HBV DNA but persistent ALT elevation. In April 2007, he presented with jaundice, ascites, and abdominal pain, developed septic shock from spontaneous bacterial peritonitis. Despite aggressive and appropriate care, he continued to deteriorate clinically and expired.

This case demonstrates 4 important points: (1) Patients with cirrhosis and drug-resistant HBV can develop life-threatening hepatic failure while on therapy, and should be closely monitored. Genotypic mutation analysis should be considered before starting a new drug; (2) Patients with LVDr substitutions are at higher risk of ETV resistance than nucleoside naïve patients, even if ETV is initiated years after LVD is stopped; (3) The I169I/T mutation has been reported to result in viral breakthrough when it coexists with additional entecavir-specific mutations along with LVDr substitutions M204V and L180M. This case suggests that LVDr substitutions plus the I169I/T mutation alone or possibly combined with the T184L polymerase mutation can result in clinical resistance; (4) This patient had HBeAg-positive HBV, but had a G1764A BCP mutation associated with decreased HBeAg production. This suggests infection with a subpopulation of mixed wild-type and pre-core/core-promoter mutant HBV, which may increase risk of virologic relapse when treatment is stopped, as seen in HBeAg negative patients.

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#### Use of Endoscopic Ultrasound Guided Fine Needle Aspiration (EUS-FNA) with Aspirate Parathormone (PTH) Assay To Diagnose Mediastinal Parathyroid Adenomas

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Rarely, patients with recurrent hyperparathyroidism have mediastinal parathyroid adenomas. These lesions often difficult to diagnose, requiring multiple sophisticated localization techniques. We describe our experience with diagnosing two patients with mediastinal parathyroid adenomas using EUS-guided FNA cytology combined with parathormone assay on the aspirate sample.

**Case 1:** A 54-year-old white male had a persistently elevated serum calcium and PTH level despite removal of a right inferior parathyroid adenoma. Sestamibi CT subsequently revealed a mass superior to the azygous vein. Radial EUS confirmed the presence of 3 cm solid/cystic lesion which on subsequent EUS-FNA showed epithelioid proliferation consistent but not diagnostic of a parathyroid adenoma. However, PTH assay performed on an aspirate sample diluted in 3 ml of saline was positive at 1800 pg/mL. Pathology of the resected specimen revealed a 29.7 g parathyroid adenoma.

**Case 2:** An 86-year-old African-American female had recurrent hyperparathyroidism following removal of a left superior parathyroid adenoma. Chest CT scan revealed enhancing nodule within the right superior mediastinum. EUS-FNA showed a 0.6 × 2.0 cm right paraesophageal lesion which cytologically showed scant epithelioid cell groups. PTH assay on the diluted aspirate was diagnostic at 6905 pg/mL. She is being managed medical at present.

**Discussion:** Preoperative localization of recurrent or persistent hyperparathyroidism is often a difficult clinical problem. Transcutaneous ultrasonography (TUS), CT, MRI, thallium-technetium, and sestamibi scans have all been used with predictive values ranging from 40 to 80%. First described by Doppman in 1983, TUS of suspicious neck lesions with concomitant PTH assay of the aspirate has become increasingly useful with sensitivities between 70–100% and a specificity of 100%. Using EUS-FNA with PTH assay on the aspirate in suspected mediastinal parathyroid adenomas is a logical extension of this technique. To our knowledge, these cases represent the first reported examples of this technique. We suggest that this procedure may be useful in definitively diagnosing patients with suspected mediastinal parathyroid adenomas.

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#### Wireless Capsule Endoscopy To Assess Extent of Small Bowel Involvement in Metastatic Melanoma

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A 58-year-old man with metastatic melanoma to the groin presented with fatigue. He was found to be iron-deficient with a hemoglobin of 6.4 g/dL. He denied overt GI bleeding but was hemoccult positive. Upper endoscopy and colonoscopy did not reveal a bleeding source. CT scan of the abdomen and pelvis showed a stable conglomeration of lymph nodes in the left pelvis but no other abnormalities. The patient was transfused 2 units of packed red cells and started on chemotherapy. His fatigue and transfusion-dependence persisted, so another CT was obtained 8 weeks after the original scan. This study revealed stable pelvic disease but also 2 new masses in the left upper and right lower abdomen measuring 6 × 5.3 cm and 3.9 × 4.5 cm respectively consistent with metastases.

He was referred for possible surgical resection, and a wireless capsule endoscopy (WCE) was performed to assess the extent of small bowel involvement. This study showed two large masses in the mid-small bowel corresponding to those seen on CT. Both lesions were multi-nodular with superficial ulcerations. A smaller mass not visualized on the CT scan was found in the distal small bowel. Several areas of lymphangiectasia were identified throughout the small bowel suggestive of other sites of metastatic disease. Given the diffuse involvement, the patient did not undergo surgical excision and will receive chemotherapy and transfusions as needed.

Malignant melanoma is the most common disease to metastasize to the GI tract. In autopsy series, GI involvement is found in almost 60% of cases, though less than 5% of cases are diagnosed antemortem. While metastatic melanoma has a 5-year survival of only 6%, studies have suggested a significant improvement in survival for patients who undergo curative surgery. Therefore, timely and accurate diagnosis of GI involvement is paramount. Prior to the advent of WCE, diagnosis relied on radiologic and/or endoscopic studies with CT scan being the most accurate diagnostic modality. However, as described in this case, CT may be insensitive to changes associated with early mucosal infiltration and small masses. Findings of diffuse small bowel involvement on this patient's WCE were critical in deeming him a poor candidate for surgical cure. Thus, the patient avoided potential morbidity from a surgery that was unlikely to prolong survival and proceeded with additional chemotherapy. WCE should be considered part of the standard evaluation of patients with metastatic melanoma and GI involvement.

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#### Intracranial Hemangiopericytoma a Rare Liver Biopsy Diagnosis

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A 44-year-old man presented with cervical pain and deficits on motion and equilibrium. He has a past history of a cerebellopontine angle meningioma surgically removed 11 years ago and more recently, he has been under oral hipocoagulation for a venous thrombosis.

Patient was admitted for evaluation: head and cervical MR imaging detected a large recurrent cerebellopontine tumor and a C4 bone lesion; thoracic, abdominal and pelvic CT scan imaging revealed numerous hepatic and vertebral secondary lesions. In this sequence a percutaneous US-guided liver biopsy was performed and histological diagnosis was hemangiopericytoma. Histological reassessment of the first cerebral tumor demonstrated the same characteristic features. This case was then interpreted as an intracranial recurrent meningeal hemangiopericytoma with extraneural liver and bone metastasis and a paraneoplastic thrombotic syndrome. For this, our patient has been treated with irradiation and is under reevaluation.

Hemangiopericytoma is an uncommon soft tissue sarcoma, and accounts for only 0.4% of primary CNS tumors having the same distribution of meningioma, these two tumors had been distinguished in 1993. Intracranial tumors rarely metastasize outside the CNS, except for meningeal hemangiopericytomas, that may undergo late recurrence, many years after the initial onset, and requires long-term follow-up.

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**Strongyloides: A Worm with Lethal Potential**

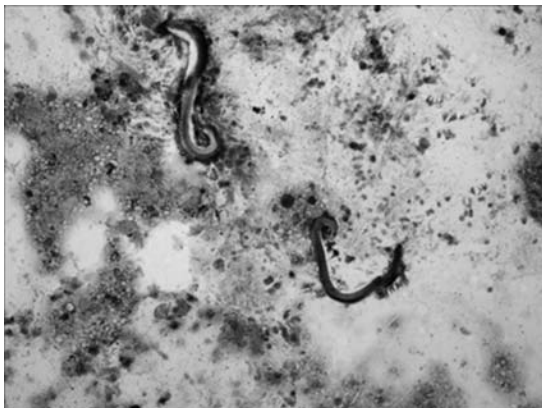
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**Introduction:** Strongyloidiasis is unique among worm infestations. It can acquire infective capacity in host's intestinal tract producing an autoinfective lifecycle, more so in immuno-compromised patients. Strongyloides hyperinfection syndrome (HS) has a mortality rate exceeding 85%.

**Case 1:** A 72-year-old Laotian male, was admitted with a four week history of profuse watery diarrhea, weight loss and abdominal discomfort. Examination was significant for hypotension, pallor, abdominal distension with hyperactive bowel sounds. Labs showed WBCs  $17.8 \times 10^9/L$ , with no eosinophils (1%). HIV serology was negative. Stool analysis revealed rhabditiform larvae of *strongyloides stercoralis* (SS) with negative stool cultures (Fig. 1).

**Case 2:** A 61-year-old, Puerto Rican male with history of SLE, on steroids was admitted with abdominal pain and fever of one week duration. He had abdominal distension, generalized tenderness and hypoactive bowel sounds. Labs showed WBCs of 7.1 cc/mm with eosinophils of 12%. CT showed dilated loops of jejunum. Emergent laparotomy was done which was negative. Post operative period was complicated by *enterobacter* septicemia, GI bleed and ARDS requiring mechanical ventilation. BAL specimen revealed larva of SS (Fig. 2).

**Discussion:** Strongyloides HS reflects massive infection with SS with wide spread dissemination of larva throughout the body. Larval forms can persist up to 40 years after infection as demonstrated by case 1 who had migrated to US 25 years ago. The larva of SS carries enteric bacteria on their outer surfaces which can result in bacterial sepsis as demonstrated by case 2. The demographic profile of US is fast changing. Hence, physicians taking care of patients from endemic areas or those who have traveled to these areas in recent or remote past must have a high index of clinical suspicion to diagnose and treat this infection which can otherwise be fatal.[figure1][figure2]



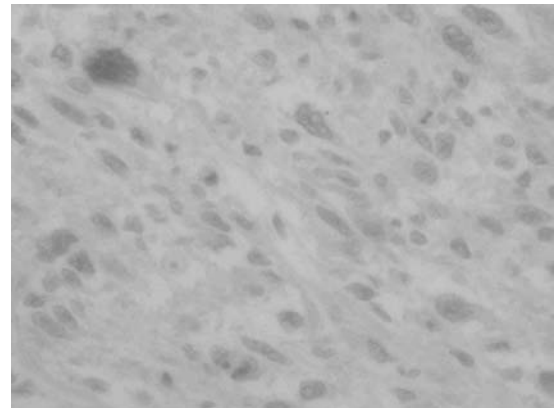
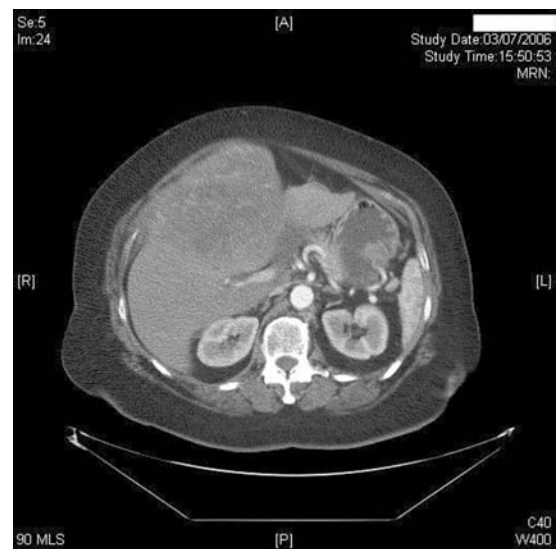
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**A Rare Liver Tumour and Rather Rare Biopsy Complication**

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Primary hepatic leiomyosarcoma is a rare tumour of the liver. It usually arises from intrahepatic vascular structures, bile ducts or ligamentum teres. We present a patient who presented with right upper quadrant mass and died of post-liver biopsy haemorrhage. Primary hepatic leiomyosarcoma was diagnosed on autopsy.

A 67 year old Caucasian woman presented to her primary physician with a three week history of abdominal pain in June 2006. She was taking aspirin, and atorvastatin. She drank little alcohol and did not use any other drugs. Examination, including breast, was unremarkable apart from a 20 cm firm, non-tender hepatomegaly. She had normocytic anaemia. Liver tests and viral serology for Hepatitis B and C were normal. Tumour markers were normal. An USS scan of the abdomen revealed an 18 cm right upper quadrant mass arising at the level of the liver. She went on to have contrast CT scan of the liver, which confirmed a mass arising from the right lobe of the liver (Fig. 1) with at least two other lesions arising from segment four and the left lobe, raising the likely possibility of hepatocellular carcinoma. An USS-guided liver biopsy was non-diagnostic and the patient, unfortunately, suffered a terminal haemorrhage following the procedure. Autopsy was carried out and histology of hepatic mass confirmed the lesion to be primary liver leiomyosarcoma (Fig. 2).



Primary hepatic leiomyosarcoma although rare should be considered in the differential diagnosis of patients with large hepatic mass in absence of cirrhosis and other risk factors for hepatocellular carcinoma. Furthermore it highlights the still appreciable biopsy related morbidity and mortality, particularly in patients with large hepatic masses.[figure1][figure2]

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### Fatal Lactic Acidosis Associated with Combination Oral Antiviral Therapy for Hepatitis B Reactivation Following Chemotherapy

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**Introduction:** Reactivation of Hepatitis B virus (HBV) infection following the administration of chemotherapy is a potentially lethal complication. Oral HBV antiviral medications are generally very well tolerated and can be used both prior to chemotherapy and to treat the actual reactivation. We report a case of HBV reactivation from chemotherapy and a potentially fatal complication of the treatment.

**Case Report:** A 54 y/o Croatian male with chronic lymphocytic leukemia (CLL) developed severe hepatitis one week after chemotherapy. He had no known history of liver disease, family history of liver disease, alcohol use, or use of other medications. All prior LFTs were normal, with no prior testing for viral hepatitis. Admission examination revealed jaundice. Laboratory data showed a protein 5.4 mg/dL, albumin 2.7 mg/dL, alkaline phosphatase 112 U/L, bilirubin 20.9 mg/dL, AST 2853 U/L, ALT 3521 U/L, and an INR of 1.76. Electrolytes, kidney function, and abdominal ultrasound were all normal. Hepatitis B surface antigen and HBV-DNA were found to be positive. Serologies for other viral infections and autoimmune hepatitis were negative. A diagnosis of HBV reactivation was made, and therapy with entecavir, adefovir, and prednisone was begun. Liver biopsy revealed severe hepatitis, cholestasis, cirrhosis, and positive HBsAg immunostaining. His laboratory values improved, and he was discharged home after a 12 day hospitalization. Ten days later, the patient presented with shortness of breath. He was hypotensive, hypoxic, coagulopathic (INR 4.4), in renal failure, with a profound metabolic lactic acidosis. LFTs revealed bilirubin 32.7 mg/dL, AST 141 U/L, and ALT 264 U/L. There was no clinical evidence of a perforated viscus. He was intubated, dialyzed, given broad spectrum antibiotics, and adefovir and entecavir were discontinued. The patient expired within 24 hours. Autopsy failed to provide any gross explanation for his lactic acidosis, and all growth from blood cultures was negative.

**Discussion:** This case report illustrates that reactivation of HBV after chemotherapy remains a major clinical issue. Prior to chemotherapy, patients should undergo testing for HBV. This case may also illustrate a rare but fatal side effect of HBV nucleoside/nucleotide analogues: lactic acidosis due to mitochondrial toxicity. Clinicians should be aware that significant side effects can occur with oral HBV antiviral agents.

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### Rare Extra-Intestinal Manifestation of Ulcerative Colitis

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A 20 year old black male with acne and severe steroid dependant UC for 8 years was admitted for worsening diarrhea after failure to taper steroids. He was previously doing well on 6-MP, steroids and mesalamine. Other symptoms included worsening facial and body pustular acne and localized anterior chest wall swelling. These symptoms were also present during his last colitis flare and resolved upon improvement of colitis.

Physical exam revealed a striking 4 cm tender, fluctuant swelling over the right sternal manubrium. He exhibited mild abdominal tenderness and severe facial and truncal pustular acne. Chest CT scan was consistent with osteomyelitis of right clavicle at the sterno-clavicular joint and fluid collection in the joint space. Subsequent CT-guided aspiration was performed and

patient was started on broad-spectrum antibiotics for presumed infectious osteomyelitis. However, Gram stain was negative and no growth in bacterial, fungal, or AFB cultures was detected suggesting diagnosis of sterile osteomyelitis and antibiotics were discontinued. The patient's clinical, radiological and histopathological features led to a conclusive diagnosis of synovitis-acne-pustolosis-hyperostosis-osteitis syndrome (SAPHO), a rare extra-intestinal manifestation of IBD. In this patient SAPHO was also present during previous colitis flares and paralleled severity of disease, resolving upon remission of colitis. The patient was initiated on infliximab therapy for both steroid dependent UC and SAPHO syndrome with good clinical response.

The acronym SAPHO was proposed in 1987 to designate a clinical and radiological entity combining skin, bone and joint manifestations. A major component is an inflammatory osteitis with negative cultures and main site for inflammation is the anterior chest wall. There is an association with HLA B27 positivity suggesting a link between the SAPHO syndrome and the spondyloarthropathies. The first line treatment of SAPHO syndrome is with NSAIDs and analgesics. Other regimens include sulfasalazine, methotrexate and TNF- $\alpha$  inhibitors. In our patient, we chose to institute TNF- $\alpha$  inhibitor therapy with infliximab because of the patient's steroid dependent UC, failure to improve on immunomodulator therapy and concomitant SAPHO syndrome. The association of SAPHO syndrome and IBD is recognized but reports are extremely rare.

In summary, the SAPHO syndrome is a rarely documented entity and must be considered in the differential diagnosis when evaluating patients with extra-intestinal manifestations of IBD.

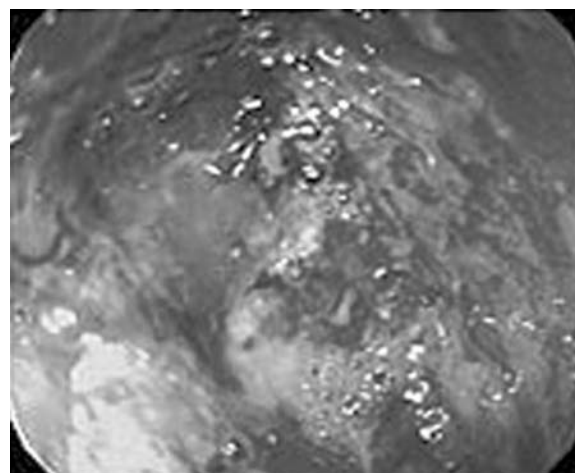
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### Extraluminal Source of Upper Gastrointestinal Bleeding

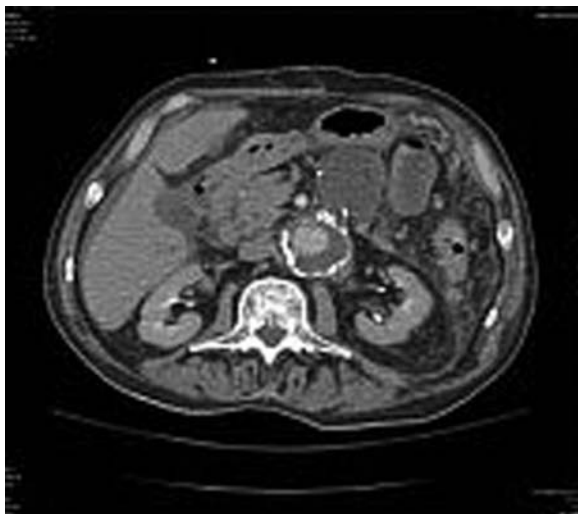
Kiran Jagarlamudi, MD\*, Rodney Eddi, MD, Walid Baddoura, MD, Alexis Bobila, MD. *Gastroenterology, St. Joseph's Regional Medical Center, Paterson, NJ and Seton Hall University School of GME, South Orange, NJ.*

Upper gastrointestinal (UGI) bleeding has many etiologies. We present a unique case of UGI bleeding secondary to an extraluminal source.

A 79 year old Caucasian male presented twenty days after an abdominal aortic aneurysm (AAA) repair, with a one-day history of several episodes of black tarry stools, fatigue and dizziness. He denied abdominal pain, nausea or vomiting. Vital signs were stable. Abdominal exam was completely benign. Rectal exam revealed black stools. He was started on an IV proton pump inhibitor. Labs showed: Hb = 8.7, BUN/Cr = 25/1.2. CT scan of abdomen was significant for a contained air-fluid collection adjacent to the proximal duodenum. Endoscopy revealed clotted blood in the stomach, and a large cavity in the distal duodenal bulb with clots but no active bleeding. Bile was noted in the distal duodenum. On the following day, the patient developed large amount of bright red hematemesis which prompted emergency surgical



exploration. There was a large perforation of the proximal duodenum. Upon evacuation of large clots from the periduodenal collection, active bleeding was noted to be originating from the right gastric vein located on the serosal surface. Suture ligation of the superior duodenal artery and right gastric vein was performed, followed by closure of the duodenal perforation using an omental patch.[figure1][figure2]



This case illustrates a unique presentation of UGI bleeding. It is likely that the patient- post AAA repair-developed a contained perforated duodenal ulcer, thus accounting for paucity of symptoms. It is not clear what initiated the serosal venous bleeding, but acid and pepsin might have played a role. To our knowledge, this is the first such reported case.

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#### Transient Pancreatic Hiatal Herniation Causing Acute Pancreatitis

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Herniation of the pancreas through a diaphragmatic hiatal hernia is an extremely rare condition reported in only three cases worldwide, of which two resulted in acute pancreatitis. Our case describes a transient herniation of the pancreas that presented with acute pancreatitis.

A 68 year-old man with a prior history of uncomplicated hiatal hernia presented with an ill-defined epigastric discomfort associated with intractable nausea and numerous episodes of non-bilious vomiting. Physical exam was unremarkable. Laboratory workup suggested acute pancreatitis. Abdominal



CT revealed partial pancreatic (body and tail) herniation into the upper mediastinum along with a complete herniation of the stomach and transverse colon. A prior CT had showed only an isolated hiatal hernia without any evidence of pancreatic displacement. The hospital course was complicated by sepsis and dehydration. A repeat pre-operative CT showed the pancreas to be intra-abdominally located. The patient underwent laparoscopic reduction of the hernia with partial gastric fundoplication. The post-operative course was uneventful.[figure1]

Hiatal hernia is commonly defined as the protrusion of the upper part of the stomach into the thorax through a tear or weakness in the diaphragm. Though the herniation of abdominal organs such as colon, small intestine and spleen have been well described, pancreatic involvement is rare. Although total or partial gastric outlet obstruction may complicate a large hiatal hernia, one has to entertain the rare possibility of pancreatic herniation with or without pancreatitis, as exemplified by our case.

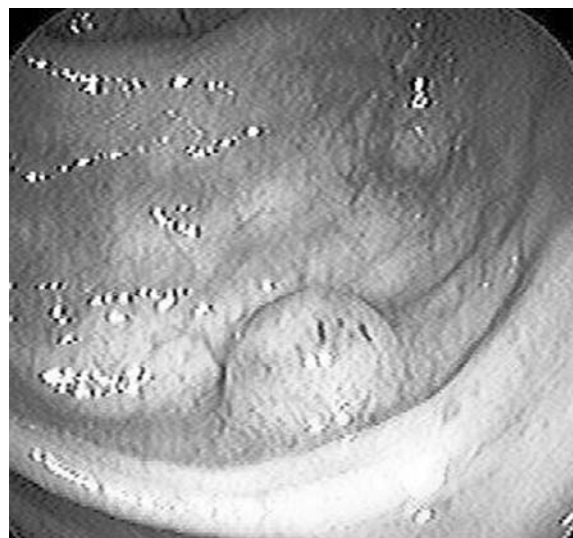
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#### Infiltrating Ductal Breast Carcinoma Metastasis to Rectum, an Uncommon Occurrence

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Breast cancer is the most common cancer and the second most common cause of cancer-related mortality in women in the US. Breast carcinoma usually metastasizes to local and regional lymph nodes, bone, lung, brain, liver, adrenal glands, and pleura. However, metastasis to GI tract structures other than liver and peritoneum is an extremely uncommon occurrence. We present a case of established infiltrating ductal carcinoma of the breast with metastasis to the rectum.

A 55 year-old African-American woman presented with complaints of nausea, vomiting of 2 days duration and constipation. The patient's medical history was significant for left breast cancer initially diagnosed by biopsy. Neoadjuvant therapy was given followed by simple extended mastectomy. Pathology revealed moderately differentiated infiltrating ductal carcinoma with negative lymph nodes. Two months later, after restaging PET scan had demonstrated multiple metastases to the ipsilateral lymph nodes, lung parenchyma and chest wall, chemotherapy was started. Abdominal examination was unremarkable; stool was occult-blood positive. CT of abdomen was normal. A colonoscopy revealed two small sessile polyps in the ascending colon and rectum, respectively, with resultant polypectomy. Pathology and immunohistochemistry of the rectal polyp showed poorly differentiated infiltrating ductal carcinoma, consistent with metastatic breast cancer.[figure1]



Eighty percent of invasive breast cancers are ductal, but distant metastasis to unusual locations such as peritoneum, meninges and the gastrointestinal tract is more frequently seen with infiltrating lobular carcinoma. In one series of 41 patients, GI metastasis in patients with invasive lobular carcinoma was twice as much as in cases of invasive ductal carcinoma (34% vs 17% respectively). Rectal involvement by breast cancer is very rare and represents the least frequent metastatic site in the GI tract. Systemic treatment with hormonal and/or chemotherapy is usually the only option in these patients because of multi-organ involvement.

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### Autoimmune Pancreatitis Masquerading as Pancreatic Cancer

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Autoimmune pancreatitis (AIP) is a rare form of pancreatitis with mild attacks of abdominal pain, pancreatic enlargement, and changes of the pancreatic duct (PD) and CBD. We present a case of AIP mimicking a cholangiocarcinoma.

A 50 year old female presented with 5 days of scleral icterus, pruritus, malaise and fatigue. She denied nausea, vomiting, weight loss, or abdominal pain. Vitals were stable and physical exam was benign.

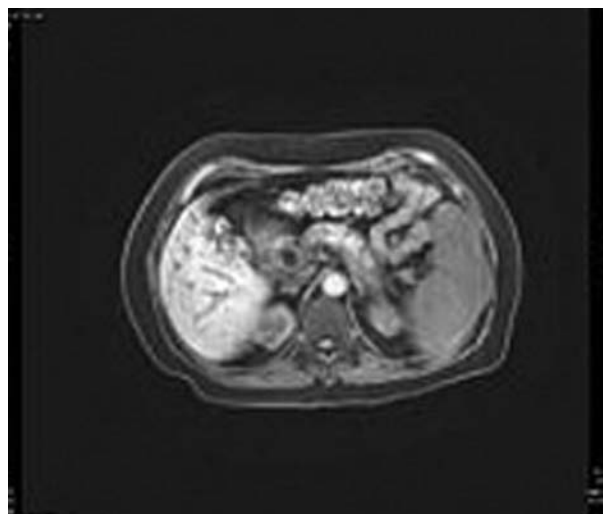
Labs showed T. Bili 8.14, AP 562, GGT 286, AST 264, ALT 427, Amylase 46, Lipase 18, ANA negative, pANCA < 1:20, and ASMA 9 (negative).

Abdominal ultrasound described a heterogeneously enlarged pancreatic body, and a 1 cm common bile duct. MRI showed diffusely enlarged and heterogeneous pancreas with CBD obstruction at the pancreatic head. ERCP revealed dilated CBD with a distal 4 cm stricture. After sphincterotomy a biliary stent was placed and antibiotics were begun. Fragments of fibroadipose tissue with lymphoplasmacytic cells and few eosinophils, without evidence of lymphoma were seen on pancreatic biopsy.

A trial of prednisone 40 mg daily was started and remarkable improvement was noted within weeks, with jaundice resolution and normalization of LFTs. Repeat imaging studies, including ERCP showed a normal pancreas and CBD.[figure1][figure2]



AIP is a chronic pancreatic inflammation characterized histologically by lymphoplasmacytic inflammation. Elevated IgG and IgG4 are useful diagnostic markers. Imaging studies reveal pancreatic swelling with narrowing of the PD and distal CBD. Whenever considering either cholangiocarcinoma



or pancreatic cancer, AIP must be included in the differential diagnosis to avoid unnecessary surgery. The dramatic response to oral steroids is the most useful clue to the diagnosis of AIP, leading to reversibility of pancreatic morphology and dysfunction.

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### Prurigo Nodularis in a Patient with Hepatic Sarcoidosis

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Prurigo Nodularis (PN) is a rare skin condition characterized by multiple pruritic hard crusty excoriated nodules. PN is the end result of chronic scratching which induces nerve thickening and eventually results in permanent skin changes, including nodular lichenification, hyperkeratosis, and hyperpigmentation. The true cause of this condition is unknown. Factors triggering PN include HIV and other immunodeficiency diseases, liver failure, renal failure, psychiatric illness, and skin diseases.

A 41-year old female with a past medical history significant for sarcoidosis of the lung and liver of ten years duration presents with a two year history of chronic intense pruritis refractory to treatment with topical steroids and ursodiol. A liver biopsy two years prior revealed hepatic granulomas consistent with sarcoid of the liver. Physical examination was significant for jaundice and diffuse, hyperpigmented, firm, scaly, and excoriated lesions on the arms, legs, and torso. Laboratory studies revealed increased alkaline phosphatase and bilirubin with mild elevations in transaminases. Extensive workup for cholestasis included negative auto-antibodies, negative viral hepatitis markers, normal ERCP, and inconclusive imaging studies. A repeat liver biopsy showed chronic hepatitis, piecemeal necrosis, and moderate fibrosis. Punch biopsy of the skin showed changes consistent with PN.

A variety of systemic conditions have been reported to be associated with PN, amongst which is liver disease. Nerve growth factors have been implicated in the pathogenesis. Topical or intralesional glucocorticoids are considered to be first-line therapy. Other options include topical vitamin D3, topical capsaicin, cyclosporin and thalidomide which can improve both appearance of the skin and pruritus.

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### Large Descending Colon Lipoma Causing Intussusception and Mimicking Malignancy

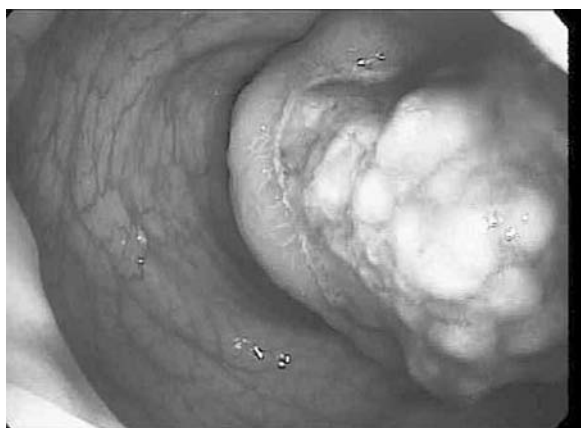
*Patrick D. Martin, MD, Bradford Sklow, MD, Douglas G. Adler, MD\*. Gastroenterology, University of Utah, Salt Lake City, UT.*



**Presentation & History:** A 69-year-old previously healthy male presented with a 1-month history of hematochezia and 10 lb wt loss. The patient denied any changes in bowel movement frequency; he continued to average 1–2 bowel movements per day. The patient denied abdominal pain, nausea or vomiting. Previous medical history included an appendectomy and hernia repair, ankle fracture. The patient took no medications, and denied any behavioral risk factors. Family history revealed a daughter with ulcerative colitis, and no colorectal cancer.

**Physical Exam & Laboratory Evaluation:** Physical exam was unremarkable. The complete blood count and the basic metabolic panel were normal. CT revealed a mass in the descending colon with partial intussusception involving the sigmoid colon, suggestive of carcinoma. There was no adenopathy or evidence of metastases.

**Treatment & Hospital Course:** Colonoscopy revealed a 7 cm, pedunculated, ulcerated, fungating mass with partial intussusception just distal to the splenic flexure at 70 centimeters from the anal verge. Biopsies only revealed inflammation.[figure1]A repeat colonoscopy was performed and the lesion was removed with a large snare and electrocautery. Pathology revealed a lipoma with no evidence of malignancy. The patient has done well thereafter.



**Discussion:** This case is unusual for several reasons: First, colonic lipomas are comparatively rare, with a reported incidence less than 5%. Second, colonic lipomas are positively correlated with distance from the anus. Our patient's lipoma was found in the descending colon. Third, colonic lipomas are most frequently small and asymptomatic. Lipomas larger than 2 cm are more often symptomatic, potentially causing obstruction, bleeding, or—very rarely—intussusception. Our patient had both a symptomatic and intussuscepted lipoma. Fourth, grossly, lipomas are generally covered by smooth mucosa. Our examination revealed an ulcerated fungating mass that appeared grossly malignant.

Large lipomas associated with intussusception are not easily differentiated from malignancies. Our experience shows that lipomas with unexpected gross appearance can also be easily mistaken for malignancy.

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#### Recurrent Gastric Telangiectasias Despite Argon Plasma Coagulation in a Patient with Osler-Weber-Rendu Syndrome

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Osler-Weber-Rendu syndrome is an inherited disorder characterized by recurrent bleeding of mucocutaneous telangiectasias. Argon plasma coagulation (APC) has been used successfully to treat lesions in the gastrointestinal tract. Here, we report a case of bleeding gastric telangiectasias with an unusual pattern of recurrence.

A 71 year-old woman with known Osler-Weber-Rendu syndrome has been followed in our clinic for over four years. She has a long history of iron

deficient anemia due to intermittent bleeding from gastric telangiectasias. Over the last three years, she has required periodic blood transfusions to maintain a stable hematocrit despite APC of these lesions every one to two months.

Multiple telangiectasias were seen in the distal half of the stomach on initial endoscopy. An ulcer later developed due to aggressive cautery. During subsequent sessions, telangiectasias were seen radiating from the periphery of this ulcer. Despite repeated APC, these telangiectasias increased in size and new ones were seen in the ulcer bed itself. With further treatment sessions, these lesions became increasingly ectatic and numerous. During her most recent endoscopic sessions, these lesions continued to bleed despite long pulses of APC. Adherent clots were seen overlying previously treated telangiectasias. At this time, the patient required two units of packed red blood cells each week to maintain a hematocrit of 28 to 30%.

Because of the failure of endoscopic therapy, the patient underwent laparoscopic partial gastrectomy with Billroth II anastomosis. The patient did well postoperatively and has not required any further blood transfusions.

APC has been used successfully to treat vascular ectasias of the gastrointestinal tract. A recent report of a patient with Osler-Weber-Rendu syndrome documented a poor response of gastric telangiectasias to APC. Although similar results were observed in this case, we have documented progression of these lesions over fourteen endoscopic sessions. This progression may represent the natural history of evolution in response to APC and may lead to insights to more effective treatment of these lesions.[figure1]



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#### An Unusual Presentation of Eosinophilic Esophagitis

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**Case Report:** A 91 year old male presented with severe dysphagia symptoms. For six years, the patient noted mild dysphagia to solids. In the three months leading up to presentation, he complained of severe difficulty swallowing both solids and liquids, with a resulting 15 pound weight loss.

The patient had a history of allergic rhinitis which flared during the spring and fall. He denied use of NSAIDs or any adverse reactions to foods. Esomeprazole was started two months prior to admission, but resulted in minimal improvement of symptoms.

Physical examination revealed an elderly male with normal vital signs. Examination of the head, neck, chest, abdomen, and extremities was normal. On upper endoscopy, the esophagus was edematous, avascular, and had a cobblestone appearance. There were diffuse white plaques and a scale-like appearance. There were no signs of stricture, mass, or external compression. Both the stomach and the duodenum were normal. Biopsies from the proximal, mid, and distal esophagus all demonstrated greater than 100 eosinophils



per high power field. The patient was diagnosed with eosinophilic esophagitis (EE). The patient was skin prick and patch tested to a panel of aeroallergens and foods. He was highly atopic to various seasonal and perennial aeroallergens. However, testing was negative to all food allergens. Treatment was initiated with fluticasone 440 mcg orally twice per day. By seven days, the patient was tolerating a regular diet with no further complaints of dysphagia.

**Discussion:** In previous case reports describing EE in adults, the mean age of the patients was younger than 50, with only four patients being older than 65. We report the first case of eosinophilic esophagitis in a nonagenarian. Endoscopic evaluation of EE typically reveals mucosal rings, corrugations, strictures, linear furrowing, mucosal fragility, and/or whitish vesicles or plaques. Our patient had a severely edematous and avascular-appearing esophageal mucosa with an overlying whitish scale. Although the endoscopic findings in this case were not typical of EE, the histology was highly consistent with EE.

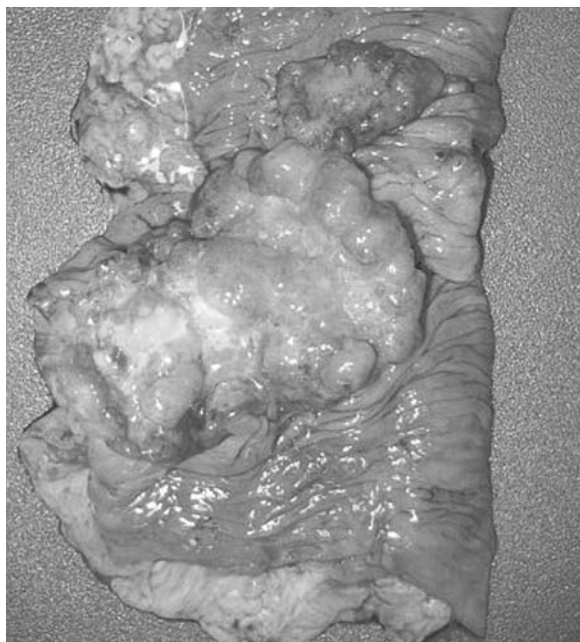
This case emphasizes that EE should be considered in the differential diagnosis of adults who present with dysphagia, regardless of their age. It also demonstrates the importance of biopsies from the proximal and mid esophagus, even if the typical endoscopic hallmarks of EE are not encountered.

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#### An Unusual Case of Three Synchronous Primary Gastrointestinal Carcinomas

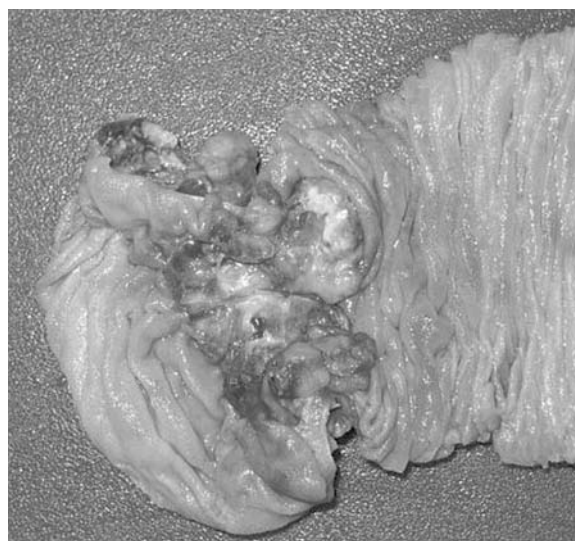
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A 57 year old man presented with complaint of on and off vomiting and 20 lb weight loss within 8 months. He was treated for prostate cancer with radiation therapy about a year ago. Family history was significant for prostate cancer in his uncle and uterine cancer in his sister in their fifties. Lab studies showed iron deficiency anemia and positive fecal occult blood test. Esophagogastroduodenoscopy was unremarkable. Colonoscopy revealed a large fungating mass in the ascending colon and biopsy showed moderately differentiated adenocarcinoma. A right hemicolectomy was performed which showed two separate tumors in the ascending colon measuring 3 cm and 6.5 cm respec-



tively, separated by 1.5 cm of normal mucosa. The postoperative course was complicated by obstipation and increased amount of nasogastric tube drainage. Computed tomography of abdomen and pelvis showed markedly distended stomach and duodenum and abrupt transition point in the proximal small bowel with no contrast beyond that level. Exploratory laparotomy showed an obstructing mass in the 3rd portion of the duodenum for which duodenectomy with primary duodenojejunostomy was performed. Pathological examination revealed a 3.5 cm circumferential obstructing adenocarcinoma of the duodenum. Tumor tissue was tested high for microsatellite instability and genetic testing showed homozygous MSH 2 mutation.

Small intestinal carcinomas are among the rarest types of cancer accounting for only 2% of gastrointestinal carcinomas. Though it is included in the tumor spectrum of Hereditary Non-Polyposis Colorectal Cancer, its incidence in those patients is rare. To the best of our knowledge, this is the first case report of three synchronous primary gastrointestinal carcinomas. [figure1][figure2]



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#### Localized Aspergillus Esophagitis: A Difficult Diagnosis of Persistent Odynophagia Leading to a Diagnosis of AIDS

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A forty-seven year old African American female without any significant medical history presented complaining of a one week history of odynophagia, weight loss, and subjective fevers. A barium swallow study demonstrated five millimeter ulcers throughout the esophagus. Esophagogastroduodenoscopy (EGD) showed white plaques throughout the esophagus. Brushings were performed which suggested Candidiasis. The patient was treated with fluconazole for ten days but without any relief. After two weeks of persistent and worsening symptoms including continued weight loss, repeat EGD showed continued white plaques throughout the esophagus. Multiple biopsies were performed which revealed numerous diffuse narrow angle branching hyphae within the esophageal mucosa consistent with Aspergillus. There were no signs of any disseminated disease. On further work-up, the patient was diagnosed with AIDS with a CD4 count of one. An increased dose of fluconazole was continued for two weeks with improvement in symptoms and HAART therapy for HIV/AIDS was initiated. Disease due to tissue invasion by Aspergillus is uncommon and occurs primarily in the setting of immunosuppression. Gastrointestinal disease secondary to Aspergillus is usually seen only in the most severely immunocompromised patients, especially those with prolonged severe neutropenia. While gastrointestinal tract

involvement is not uncommon in the context of disseminated disease, it is **rarely a localized site** of infection. In a series of 3374 autopsies including a large proportion of cardiac and oncology patients, Young et al observed invasive aspergillosis in ninety-eight cases with gastrointestinal tract disease in twenty-one percent. In one series approximately one-third of cases with disseminated aspergillus infection had gastrointestinal involvement including esophageal lesions in five cases, with no localized gastrointestinal infection. The histological appearance of typical fungal hyphae with associated tissue damage is sufficient for definitive diagnosis of invasive fungal infection in accordance with published guidelines. We present a **rare case of localized gastrointestinal invasive aspergillosis** in the absence of disseminated disease.

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#### A Rare Case of Metastasis-Induced Acute Pancreatitis in a Patient with Small Cell Carcinoma of the Lung

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Acute pancreatitis caused by metastatic carcinoma to the pancreas is uncommon. We report a rare case of metastasis-induced acute pancreatitis with small cell carcinoma of the lung.

A 49 year old female, smoker, with history of small cell carcinoma with limited disease to the right lung, was admitted with constant epigastric abdominal pain radiating to the back for 4 days. The patient denied any fever, chills, or nausea. One month earlier she had completed 1 cycle of chemotherapy with cisplatin and etoposide. She denied any history of heavy alcohol use or hypertriglyceridemia.

On admission, the patient was afebrile and in mild distress. Temperature was 98.1°F, blood pressure was 127/76 mm Hg, pulse was 78/minute, and respiration rate was 20/min. Physical examination revealed mild bibasilar crackles. The bowel sounds were normoactive. Mild tenderness to palpation was noted over the mid-epigastric region without rebound tenderness, guarding, or palpable mass. Laboratory evaluation revealed a lipase of 2206 IU/dL [10–45 IU/dL], white blood cell count of  $32.3 \times 10^3/\mu\text{L}$  [4.8–11.0  $\times 10^3/\mu\text{L}$ ], and hematocrit of 29.1% [37–47%]. Liver tests and creatinine were all in normal range.

CT scan of the abdomen revealed a  $2.3 \times 2.2$  cm hypodense mass in the head of the pancreas without associated pancreatic or common bile duct dilatation. In addition, multiple small liver lesions and a moderate right pleural effusion were noted. To clarify the lesion seen on the pancreas, EUS-guided FNA of the mass in the pancreas was performed. The cytology revealed malignant cells consistent with small cell carcinoma of the lung.

The patient was managed conservatively with dietary restriction, narcotics for pain control, and parenteral fluids. Although her pain improved, serum lipase was persistently elevated up to 1000 IU/L. Subsequently, she experienced increasing shortness of breath. She elected for comfort care and died a few days later. Metastasis-induced acute pancreatitis is rare and can occur as the initial presenting manifestation of a carcinoma or late in the course of the disease. Mechanisms of acute pancreatitis in our patient is unclear but may include mass effect on the pancreas and/or mechanical pancreatic duct obstruction. Chemotherapy, surgery and endoscopic intrapancreatic stenting may be considered. However, the overall prognosis, as seen in our case, is extremely poor.

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#### Suspected Asymptomatic Large Colon Lipoma: Biopsy?

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Lipomas are the second most common benign tumors of the colon, after adenomatous polyps. Management of incidentally detected asymptomatic large colon lipomas has not been well studied. To our knowledge, this is the

first case report of asymptomatic colon lipoma that was complicated by both hemorrhage and bowel obstruction after endoscopic biopsy.

**Case report:** A 59-year-old female with history of hypertension and hyperlipidemia, underwent routine colonoscopy that showed 3.5 cm lipomatous appearing polyp in the sigmoid colon. Patient was referred to gastroenterology clinic for evaluation of the sigmoid mass. At this point, review of systems was negative. Patient had no previous surgeries and family history was unremarkable. Patient was taking Atorvastatin and hydrochlorothiazide. One year after her initial procedure, a repeat colonoscopy revealed a 3.5 cm, soft, mobile, pedunculated mass in the sigmoid colon with positive pillow sign (indents when depressed using biopsy forceps) and was biopsied with cold forceps. Histopathology revealed smooth muscle prominence and fibrovascular tissue. One week after the procedure patient presented with bright red blood per rectum and mild crampy abdominal pain. The patient was hemodynamically stable at her baseline hemoglobin level. Physical exam revealed left lower quadrant tenderness on deep palpation with no peritoneal signs. The patient underwent immediate flexible sigmoidoscopy that showed completely obstructing purplish mass in the sigmoid colon with an overlying clot. Virtual colonoscopy was performed which showed a pedunculated soft tissue density consistent with lipoma and 2.9 cm mass in the lumen of sigmoid colon consistent with hematoma. Patient was managed conservatively; bleeding resolved spontaneously and was discharged to home. During six months of follow-up patient remained asymptomatic.

**Conclusion:** Colon lipomas, can be diagnosed by colonoscopy by their characteristic features i.e, mobile, soft mass with positive pillow sign and CT scan appearance of smooth borders and uniform fat equivalent density. In our review, out of 22 colon lipoma biopsies reported in literature only 4 are conclusive with a diagnostic yield of 18%. In addition to a low diagnostic yield, biopsy may result in complications such as bleeding or obstruction. We report a novel case in which both bleeding and colonic obstruction resulted from biopsy of a large sigmoid lipoma. For this reason EUS evaluation is likely preferable to biopsy of these lesions.

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#### Consequences of a “Dropped Pass”: Liver Abscess Due to *Eikenella corrodens*

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**Case report:** A 64-year-old man presented with right upper quadrant pain and fever for 3 days and a 3 week history of malaise following laparoscopic cholecystectomy for acute cholecystitis. The operative note described gallbladder rupture and spillage and suction recovery of multiple pigmented stones. On exam, he had stable vitals and a nodular, tender liver edge 3 cm below the right costal margin. White blood cell count was elevated to  $13.2 \times 10^9/\text{L}$ . Computed tomography of the abdomen/pelvis revealed a 6 cm liver abscess in right, posterior lobe. Following percutaneous drainage, sinogram showed a large, rounded filling defect within the cavity consistent with a retained stone (Fig. 1). Abscess fluid cultures grew *Eikenella corrodens* and *Prevotella ovis*. Blood cultures were negative. Antibiotic coverage of levofloxacin and metronidazole was switched to ertapenem. The drain was removed after 18 days, and the patient completed a 1 month course of ertapenem. He reported symptom resolution, and follow-up CT demonstrated near complete resolution of the abscess.

**Discussion:** During the 375,000 laparoscopic cholecystectomies performed annually, dropped gallstones occur with a reported incidence ranging from 3–33%. Of these, the risk of complications ranges from 2.3–12% of cases, presenting 4–9 months post-operatively. Complications described include bowel obstruction, fistula, and intra-abdominal abscess. As seen in this patient, pigmented stones and acute cholecystitis are known risk factors for gallbladder rupture during laparoscopy. Yet, our patient's presentation on the 21st post-operative day makes this one of the earliest reported cases of a post-operative complication secondary to a dropped gallstone. Abscesses

associated with dropped gallstones most frequently grow *Enterococcus*, *E. coli*, and *Klebsiella*. *Eikenella corrodens* is a pathogen usually associated with bite wounds, and few examples of *Eikenella* liver abscesses exist in the literature. *Eikenella* is commonly resistant to metronidazole, making recognition of infection particularly important for adequate antimicrobial therapy.[figure1]



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#### Endoscopic Diagnosis of Boerhaave's Syndrome

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**Case Presentation:** A 78 year old male presented with chest pain and dyspnea. Four days before he underwent transrectal prostate biopsy and subsequently had gross hematuria. On the day of presentation he had micturition syncope but denied chest trauma.

Physical examination, EKG and cardiac enzymes were normal. Chest x-ray showed a layering fluid collection in the left chest. Thoracentesis revealed 600 cc of bright red blood. Chest tube was placed. The patient required mechanical ventilation and was hemodynamically unstable, prompting abortion of planned chest CT and emergent surgical exploration. Anterolateral thoracotomy revealed 1500 cc of blood clot which was removed. No significant injury, other than a bleeding needle tract from the diagnostic thoracentesis, was observed.

The patient developed massive hematemesis and an upper endoscopy showed a laceration in the distal esophagus with visualization of pulmonary tissue. Exploration through a posterolateral thoracotomy widely opening the mediastinal pleura, identified the esophageal tear which was primarily repaired in one layer. Despite critical care and multiple transfusions, the patient expired. Boerhaave's Syndrome is a barogenic rupture of the esophagus which classically has a preceding episode of emesis. Mackler's triad of vomiting, chest pain, and subcutaneous emphysema is seen in about 50%. Rapid diagnosis and treatment is essential.

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#### MRI Differentiates Anoxic Brain Injury from Liver Failure Associated Cerebral Edema in Ecstasy (MDMA) Toxicity

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"Ecstasy" (3,4 methylenedioxymethamphetamine, MDMA) is a popular recreational drug associated with acute liver failure, serotonin syndrome, rhabdomyolysis, cerebral edema, and stroke.

**Case:** An 18 year old healthy male presented with obtundation following consumption of ecstasy. On admission, he was intubated for airway protection and noted to have liver and renal failure. Laboratory testing revealed WBC  $21.3 \times 10^9/L$ , creatinine 2.1 mg/dL, INR 1.84, CPK 6000 U/L, AST 4551 U/L, ALT 3224 U/L, bilirubin 2.2 mg/dL, alkaline phosphatase 139 U/L, and Factor V 19%. ANA, ASMA, HBsAg, HAV IgM, HCV Ab, and ceruloplasmin were negative. The patient was started on N-acetylcysteine. A head CT showed well-defined, symmetric hypodensities in the globus pallidi, cerebellum, and cortex. EEG showed diffuse slowing with no seizure activity. The patient was noted to have decerebrate posturing. MRI showed bilateral restricted diffusion in the globus pallidi and subcortical white matter, consistent with irreversible cytotoxic injury rather than reversible vasogenic edema from hepatic encephalopathy. The postulated mechanism of toxicity was from direct excitotoxicity due to ecstasy. An echocardiogram did not reveal a right-to-left shunt or thrombus. The bilirubin, INR, transaminases, and creatinine normalized over seven days but the patient continued to remain comatose with decerebrate posturing. Comfort measures were instituted.

**Conclusion:** This case demonstrates a patient with MDMA toxicity who presented in liver and renal failure with a coma from anoxic brain injury. Initially, his coma was attributed to hepatic encephalopathy. He met Clichy criteria for liver transplantation: Factor V less than 20%, with grade 4 encephalopathy. However, an MRI with diffusion weighted imaging revealed irreversible brain injury and based on these findings, the patient was not listed for liver transplantation. In MDMA toxicity, excessive serotonin release may lead to cerebral vasoconstriction, stroke, and anoxic brain injury. Thus, anoxic brain injury may occur independent of acute liver failure. In MDMA associated liver failure, MRI may be useful to distinguish patients with permanent brain injury who should be precluded from liver transplantation.

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#### An Unusual Complication of Nissen Fundoplication

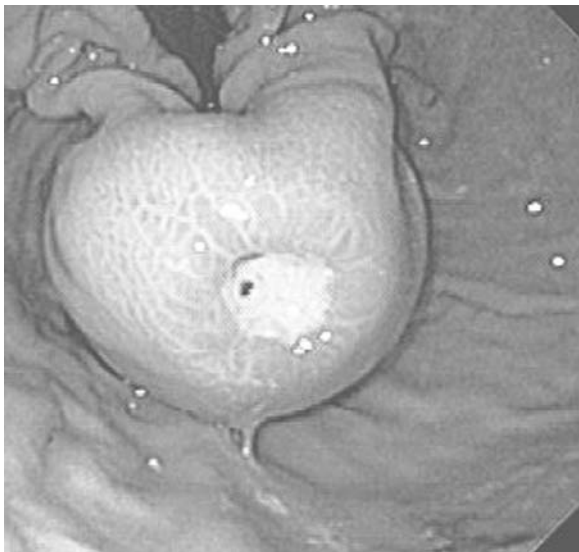
Simon C. Chan, MD, Ashok Shah, MD\*. Gastroenterology, University of Rochester Medical Center, Rochester, NY.

The Nissen fundoplication reinforces the LES by a circumferential wrap of the distal esophagus with the gastric fundus. Well known complications include post-operative dysphagia and persistent heartburn. Here we report an unusual complication in which the patient had a severe gastrointestinal bleed from an ulcer on the fundoplication wrap.

A 64 year-old man with a history of GERD and three prior Nissen fundoplications (1991, 1993, and 2003) was admitted with a four day history of dizziness and black stools. Initial bloodwork revealed a hematocrit of 32%, which fell to 19% over the course of 12 hours. Subsequent upper endoscopy the following day revealed a submucosal mass in the stomach immediately distal to the gastroesophageal junction associated with an 8 mm clean based ulcer. Because the patient was a poor historian, we were not aware that the patient had had prior antireflux surgery.[figure1] Further evaluation with a linear endoechoscope revealed a hyperechoic lesion arising from the third layer of the stomach suggestive of a lipoma or GIST tumor. The patient's hematocrit remained stable during his hospitalization and a repeat endoscopy one week later showed no significant changes in the size or appearance of the lesion or ulcer.

One month later, the patient had a repeat endoscopy. Examination of the gastric cardia revealed a swirl of gastric folds associated with a Nissen fundoplication. Examination with a radial echoendoscope revealed multiple gastric layers associated with such a wrap.

There are rare case reports of gastric ulcers following a Nissen fundoplication. These ulcers often occur in the proximal stomach (an exceptionally unusual location) and is thought to be a result of anatomical distortion of the fundoplication. Here we observed an ulcer located on the fundoplication wrap itself, resulting in gastrointestinal bleeding. To our knowledge, this



is the first report of such a complication. We suspect that fundoplication wrap may have been misidentified initially due to bleeding within the gastric submucosa and distention of a gastric fold with subsequent mass-like appearance. The cause of the ulcer is likely local mucosal ischemia.

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#### **An Unusual Case of Heterotopic Gastric Mucosa Followed for 5 yrs**

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Heterotopic gastric mucosa is either a result of abnormal differentiation of fetal endoderm or a metaplastic process from regeneration of local mucosa. It can occur throughout the GI tract, most commonly in the esophagus and meckels diverticulum. Review of literature suggests duodenal heterotopic gastric mucosa is fairly rare, usually associated with an ulcer and ranges in size from 3 mm to 10 mm. Here we illustrate a case of a duodenal heterotopic gastric mucosa not associated with an ulcer measuring 40 mm. An 89 yr old caucasian male, was admitted for constipation and anemia. Pertinent positive findings on physical examination was a positive stool hemocult on digital rectal examination. Lab data showed Hb-11.9 mg/dl. CT of the abdomen and pelvis was negative for any pathology. EGD revealed 40 mm sessile polyp in the duodenal bulb with an associated esophageal ulcer, hiatal hernia, atrophic gastritis and grade III esophagitis. Multiple biopsies were taken but the polyp was not removed. The pathological report showed heterotopic gastric mucosa. Interestingly, approximately 5 years ago this patient underwent EGD which reported a flat sessile soft villous 10 mm polyp in the duodenal bulb. Biopsy report was the same. The pathogenesis of gastric gland heterotopia is controversial. Some investigators advocate a theory of secondary invasion of the surface mucosa through a defect in the muscularis mucosa, arising as a result of inflammation or ulceration, others insist on a congenital origin based on cases in which no microscopic signs of muscularis mucosal injury or inflammatory cell infiltration of the mucosal layer were demonstrable. Experimental evidence suggests that downward adenocystic proliferation of glands is a dysplastic or a precancerous change. Histology shows normal gastric mucosa including mucinous tall columnar epithelial cells, as well as chief and parietal cells below the gastric glands, just in an abnormal location. Complications include obstruction, peptic ulceration, hemorrhage and perforation. There is no reference in medical literature to malignant transformation of heterotopic gastric mucosa. Endoscopic resection, surgical resection and observation by periodic EGD have all been suggested for a follow up and differential diagnosis. To our knowledge, this is the largest polypoid heterotopic gastric mucosa in the literature and the patient was followed for 5 yrs. with significant increase in the size of the mucosa from

10 mm to 40 mm with no change in histopathology. Pictures of endoscopy will be presented.

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#### **"Downhill" Esophageal Varices Treated with Azygos Vein Embolization**

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"Downhill" esophageal varices (DEV) are varices associated with SVC obstruction and pulmonary hypertension but not with portal hypertension. We report a rare case of DEV deriving off the azygos vein in the setting of pulmonary hypertension and normal hepatic venous pressure gradient (HVP), treated with azygos vein embolization and variceal band ligation.

**Case Report:** A 55 year old female with a history of rheumatic heart disease, mechanical mitral and aortic valve replacement on warfarin presented with hematemesis. Laboratory testing revealed Hg 7.5 g/dL, INR 6, and albumin 2.5 g/dl. Band ligation was performed during upper endoscopy which revealed multiple, bleeding grade IV esophageal varices. An echocardiogram showed an ejection fraction of 65% with severe pulmonary hypertension and signs of right ventricle overload. A CT scan revealed extensive vascular changes around the distal esophagus. A transjugular hepatic venogram revealed a free hepatic venous pressure (FHVP) of 23 mmHg and a wedged hepatic vein pressure of 27 mmHg with calculated HVP of 4 mmHg. Liver biopsy revealed cirrhosis. The patient was discharged on warfarin. Ten days later, the patient presented again with hematemesis and repeat esophageal varices band ligation was performed. A direct transjugular portal venogram revealed no evidence of esophageal varices. Selective catheterization of the azygos vein demonstrated reversed azygos vein flow and large distal esophageal varices. Selective embolization and coil placement of the right and left azygos vein was performed. A EUS confirmed massive paraesophageal varices with a markedly dilated azygos vein and thoracic duct. The patient has remained on warfarin with no further bleeding episodes three months after discharge.

**Discussion:** DEV are so labeled because the direction of flow is "downhill" or retrograde towards the azygos vein from the submucosal venous network around the esophagus which forms in response to obstruction of the SVC or pulmonary hypertension. This is in contrast to esophageal variceal bleeding associated with portal hypertension which is "uphill". This case demonstrates the efficacy of combined endoscopic variceal ligation with selective endovascular azygos vein embolization and coil placement in managing DEV, a rare cause of upper GI bleeding.

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#### **A Case of 300 Pound Weight Loss, Malabsorption, Malnutrition and Protein Losing Enteropathy Due to Systemic Lupus Erythematosus of the Small Intestine**

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We report a case of very severe malabsorption and malnutrition due to Systemic Lupus Erythematosus (SLE). A 55 year-old female was transferred to our hospital, due to a three-year history of chronic diarrhea, profound weight loss of 300 lbs, and recurrent small bowel obstruction. Previously, a colonoscopy demonstrated nonspecific colitis of the ascending colon, and a trial of a gluten-free diet was ineffective. Her past medical history was significant for lysis of adhesion surgeries. On admission, physical exam revealed temporal wasting, non-patchy hair loss, anasarca, and loss of subcutaneous fat. Her BMI was 14: decreased from a baseline of 72. Presenting laboratory

findings revealed an Hgb of 10 gm/dL. CRP was elevated at 80 mg/L. Albumin was 1.7 g/dL. Zinc was 29 ug/dL. Vitamins A and D were low at 30 ug/dL and 5 pg/mL, respectively. Chemistry and hepatic profiles, amylase, and lipase were normal. CT scan revealed pleural effusions, ascites, and dilated small bowel loops. EGD demonstrated atrophied duodenal mucosa with villous blunting and few intraepithelial lymphocytes that was inconsistent with Celiac disease. The patient's condition worsened; she was intubated and transferred to the ICU. Her albumin fell to <1 g/dL and her prealbumin to 3.9 mg/dL despite being on TPN. Due to low complement levels, she underwent SLE workup. Lupus serologies revealed positive ANA titer of 1:10240; negative anti double stranded DNA; positive anti Smith antibodies at 248 U/mL. The patient had small bowel resection, due to her obstruction. Pathology revealed full thickness inflammation of the small intestine, with ulceration and myositis. Combined with her serology findings, it was concluded that she had lupus-associated enteritis. She was treated with IV solumedrol and TPN. After 5 weeks of treatment, her albumin rose to 2.2 g/dL and prealbumin to 19 mg/dL. The patient was discharged on oral prednisone and azathioprine. This case demonstrates that SLE can be a cause of profound weight loss, malabsorption, malnutrition, and protein losing enteropathy from extensive small bowel inflammation. Recognition of severe small bowel inflammation due to SLE is important for effective treatment to improve both short and long term survival.

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### Hereditary Gastric Carcinoma: At Management Cross Roads

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**Introduction:** Hereditary diffuse gastric cancer (HDGC) is an autosomal-dominant cancer susceptibility syndrome characterized by early onset diffuse gastric cancer and lobular breast cancer. Germ-line truncating mutations in the E-cadherin gene (CDH1) have been shown to underlie about 30% of HDGC families of various ethnic backgrounds. Here, we report a family with HDGC.

**Case 1:** A 69-year-old, female with a history of familial gastric and breast carcinoma, was diagnosed with lobular carcinoma of right breast at 43 years of age. Genetic screening for BRCA1 and BRCA2 was negative. Full sequencing of CDH1 gene done last year was positive for 2287G>T deleterious mutation. Since then she is under chromoendoscopic surveillance at six monthly interval, as she is still weighing the offer of prophylactic gastrectomy. Detailed family history was obtained and pedigree constructed (Fig. 1).

**Case 2:** A 55-year-old, female presented for consultation about being tested positive for CDH1 gene mutation. She was found to be the first cousin of case 1 and having same deleterious mutation of CDH1 gene at the same locus. She underwent EGD and was discovered to have linitis plastica with histology revealing invasive, poorly differentiated adenocarcinoma, signet cell type. Patient is now ongoing evaluation for total gastric resection.

**Discussion:** Germline CDH1-associated gastric cancer develops diffusely throughout the stomach wall and foci of malignant cells often underlie a

grossly and histologically normal surface epithelium. Therefore serial conventional EGD, chromoendoscopy or endoscopic ultrasound may not be a useful screen for this patient population. Our cases illustrate the controversies surrounding the optimal management of germline E-cadherin mutation patients and their families. The average age of onset of gastric cancer in germline CDH1-positive families is 38 years, but it has been documented in teens as well. The question arises as to what is the ideal timing for surgical intervention and screening, given our case 1 has been asymptomatic up till now but on the other hand, case 2 being already positive for malignancy.[figure1]

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### Loratidine-Induced Hepatitis with Autoimmune Features Associated with Small Fiber Peripheral Neuropathy

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**Purpose:** Loratidine-induced hepatitis is rare, with only a few case reports in the medical literature. We describe a patient with loratidine-induced hepatitis with autoimmune features, associated with small fiber peripheral neuropathy.

**Results:** A 49 year old male was previously well except for multiple environmental allergies. He had been taking loratidine 10 mg/day for 1 year. He had no other risk factors. He complained of painful paresthesiae to his lower extremities. His ALT was 492 U/L, AST 233 U/L. Extensive serologies were negative including cryoglobulins. Celiac disease was excluded by a negative celiac disease panel, normal small bowel biopsy and negative HLA DQ2 and DQ8. His only autoimmune markers were positive circulating immune complexes of 45 u/ml (normal less than 8 u/ml) and low level anti-smooth muscle antibody of 1:80. His anti-nuclear antibody, p-antinuclear cytoplasmic antibody, and antibodies to soluble liver antigen and Liver-Kidney Microsomal were negative, and immunoglobulin IgG, IgM and IgA levels were normal. HLA typing did not reveal the susceptibility alleles known to be associated with autoimmune hepatitis. Liver biopsy revealed panacinar hepatitis, grade 4/4 with no cirrhosis. Nerve biopsy and EMG/nerve conduction studies were consistent with small fiber peripheral neuropathy. Loratidine was discontinued. Despite being off loratidine for 6 weeks, his liver biochemistries progressed to an ALT of 772 u/ml, AST of 277 and bilirubin of 1.9 mg/dL. He was treated with prednisone 40 mg/day and pregabalin 75 mg bid. His liver biochemistries rapidly normalized. Prednisone was gradually tapered and discontinued after 1 year. There has been no recurrence of hepatitis after 20 months of observation. He remains with symptomatic peripheral neuropathy.

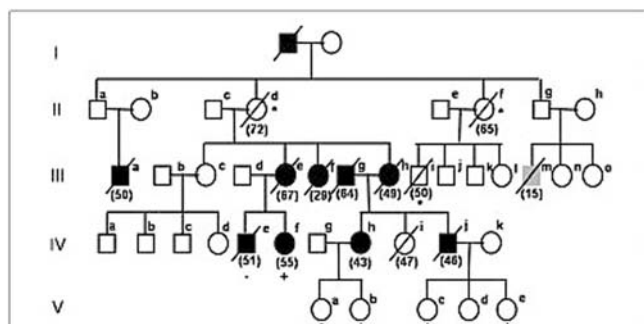
**Conclusion:** We describe a rare case of loratidine-induced hepatitis with autoimmune features associated with small fiber peripheral neuropathy. Immune features included circulating immune complexes, low titer anti-smooth muscle antibody, and rapid response to corticosteroids. We speculate that loratidine caused an immune mediated hepatocellular injury and peripheral neuropathy.

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### Leakage from Surgical Jejunostomy Tube Due to Sharp Angle of Effluent Limb

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**Purpose:** 30 year old male with mental retardation, cerebral palsy and seizures was admitted in October 2004 for respiratory distress from pneumonia. He was intubated and after extubation, he developed dysphagia. A gastroenterologist attempted percutaneous endoscopic gastrostomy tube (PEG) placement but was unsuccessful since no transillumination was seen. Surgery was then consulted. They tried to do an endoscopic PEG in the operating room without success. Upon laparotomy the stomach was found to be higher



than normal in the area under the costal margins and could not be pulled down. After multiple attempts to reposition the stomach, PEG placement was determined to be impossible due to a result of increased tension on the stomach. A jejunostomy tube was therefore placed 20 cm distal to the ligament of Treitz.

The patient has had about 30 feeding tube changes over the following 3 years due to chronic tube leakage. He suffered from extensive skin breakdown and infections surrounding the jejunostomy tube making it difficult for the family to take care of him. The patient's father as well as medical staff had changed the jejunostomy tubing as a standard blind procedure and time after time, leakage continued to occur. Different sized tubes were attempted without success.

When he was referred to us we took him to GI lab for endoscopic evaluation and replacement of the jejunostomy tube. After entering approximately 2 cm through the stoma with a 6 mm slim nasal upper endoscope, a division with an afferent and efferent limb was seen. The limb slightly to the right and straight ahead was assumed to be the afferent limb from the stomach. Instead we took a very sharp left turn and advanced 50 cm down with the endoscope. A Savary guidewire was placed through the scope, the scope withdrawn, and then a 45 cm jejunal feeding tube was threaded over it. Radiology confirmed that this was the efferent limb. Leakage from the feeding tube has since reduced dramatically and the skin has healed.

When jejunostomy feeding tubes repeatedly leak despite multiple tube changes, it is recommended to perform an endoscopic guided tube change with an upper nasal endoscope. In this case, during blind tube changes, the tube most likely repeatedly entered the pathway of least resistance, which was in the limb leading towards the stomach. This caused tube feeds to travel back out the tube or exit the space surrounding the tube.

## 590

### Extensive Nonalcoholic Fatty Liver Disease and Cirrhosis in a Single Family: A Case Report

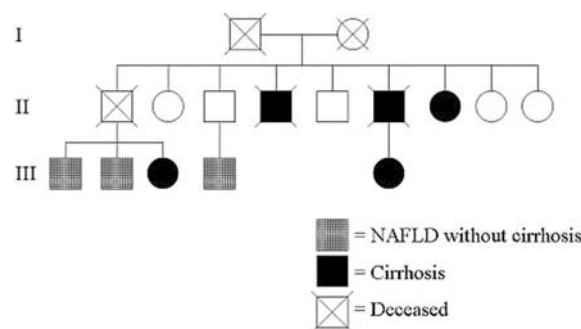
Stacy K. Tong, MD, Joseph Ahn, MD, Stanley M. Cohen, MD\*. Hepatology and Gastroenterology, Rush University Medical Center, Chicago, IL.

**Purpose:** Nonalcoholic fatty liver disease (NAFLD) is a spectrum of disease ranging from simple fatty liver to nonalcoholic steatohepatitis (NASH) to cirrhosis. NAFLD appears to be the most common liver disease in the United States, and may have a higher prevalence within certain families, suggesting a role for genetics. Prior studies have shown that up to 18% of NASH patients had an affected 1st-degree relative. The limited prior case reports of familial clustering only showed a small number of affected family members. We present a family with extensive disease involvement.

**Case report:** A 62 year-old patient with cirrhosis who had undergone orthotopic liver transplantation, reported an extensive family history of liver disease. The family tree illustrated below represents the entire 1st and 2nd generations of the family as well as the affected members of the 3rd generation. We identified 8 members (5 male, 3 female) of this family with NAFLD or cirrhosis. The affected family members span two generations. Three of the family members had uncomplicated NAFLD and 5 had cirrhosis. In the 2nd generation, 3 out of 9 siblings (33%) had cirrhosis. One of the 3 died awaiting liver transplant and 2 received orthotopic liver transplants. All 3 affected members of this generation were diabetic and overweight, and 2 had hyperlipidemia. There were 25 total family members of the 3rd generation and 20% (5/25) had known liver disease. Two members of the 3rd generation had cirrhosis, 1 of whom was overweight with hypercholesterolemia. The 3 non-cirrhotic NAFLD patients in the 3rd generation all had obesity and hyperlipidemia.

**Discussion:** This case illustrates an extensive family history of NAFLD and cirrhosis, exhibiting the entire spectrum of fatty liver disease. Some family members have not been evaluated for liver disease, possibly under-estimating the true prevalence of liver disease within this family. The extensive involvement described in this case report suggests a genetic predisposition

in addition to common dietary and environmental factors in this familial cluster.[figure1]



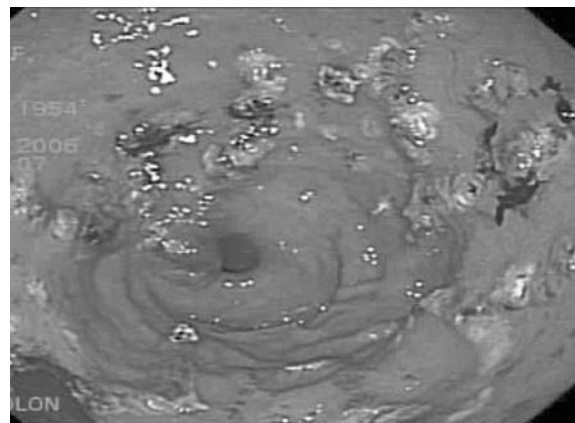
## 591

### Gastric Antral Vascular Ectasia Associated with Systemic Sclerosis: A Case Report and Review of the Literature

Sindu Stephen, MD, Marie L. Borum, MD\*. Department of Gastroenterology, George Washington University, Washington, DC.

**Purpose:** The association between GAVE and SSc have been reported infrequently in the literature with sporadic case reports. In this paper, we describe a patient with iron deficiency anemia diagnosed with GAVE and presumed SSc.

**Results:** A 51 year old male with a history of hypertension was referred to rheumatology clinic for skin thickening. Three months prior to admission, he noticed progressive skin thickening involving the anterior chest, neck and face. He also noticed some dyspnea on exertion but denied symptoms concerning the gastrointestinal tract. Review of systems was otherwise negative. On examination he had pale conjunctiva, thick skin over anterior chest, neck face and arms. His fingers revealed clubbing. Pulmonary and cardiovascular exams were unremarkable. Fecal occult blood test was positive. He was also found to be hypoxic with oxygen saturation of 90% on room air. His labs are shown in Table 1. He had a chest computed tomography which revealed interstitial fibrosis with prominence at the bases with pulmonary function tests showing a decreased diffusing capacity. An EGD was performed to investigate his anemia. The procedure revealed Gastric Antral Vascular Ectasia which was treated with argon plasma coagulation therapy. Due to his clinical skin fibrosis and internal organ involvement, he was diagnosed with systemic sclerosis.[figure1]



**Conclusion:** This case illustrates the importance of recognizing this disease as a potential cause of upper gastrointestinal bleeding and anemia in scleroderma patients. Early recognition of the association between SSc and GAVE

with prompt referral to a gastroenterologist for iron deficiency anemia in this patient population is advised.

Labs			
WBC (cells/ml)	9000 cells/ml	ANA	+1:80 speckled
Hematocrit (%)	21	ESR	45
Platelet count	652	CRP	1.6
BUN (mg/dl)	19	Rheumatoid Factor	+1:8
Ferritin (ng/ml)	7	Anti dsDNA	negative
TIBC (mcg/dl)	331	Anti Ro & La	negative
Iron (mcg/dl)	16	Anti-smooth muscle	negative
MCV	60	Anti-centromere Antibody	negative

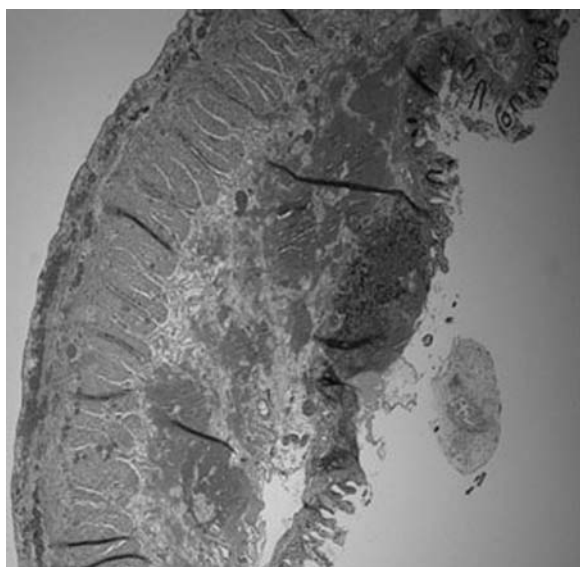
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### Ischemic Necrosis of the Terminal Ileum and Cecum with Oral Kayexalate

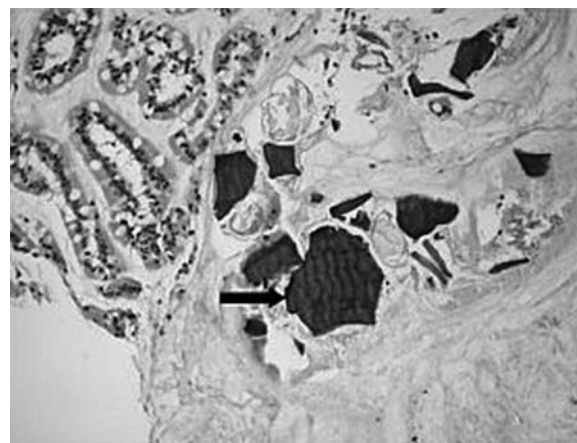
Srinivas R. Mummadi, MD, Ashutosh S. Naniwadekar, MD\*, Phong Tang, MD. Department of Internal Medicine, University of Texas Medical Branch, Galveston, TX.

**Purpose:** Sodium polystyrene sulfonate (Kayexalate) is a cation-exchange resin used with sorbitol for the treatment of hyperkalemia since 1961. There have been several case reports of colonic necrosis with the use of Kayexalate-sorbitol enemas and very rarely with oral Kayexalate. The overall incidence of Kayexalate-sorbitol induced colonic necrosis has been estimated to be around 0.27%. Clinical manifestations may vary from mild abdominal pain or gastrointestinal bleeding to bowel perforation presenting with an acute abdomen. The exact pathogenesis of Kayexalate-sorbitol induced colonic necrosis is unknown. However it is believed to occur due to severe vasospasm induced by osmotic mucosal injury from the sorbitol component, on a background of elevated renin levels in uremic patients.

A 39-year-old African American man with end-stage renal disease secondary to focal segmental glomerulosclerosis, on hemodialysis, presented to us with a syncopal episode. He had missed two scheduled days of dialysis. On physical examination, he had bibasilar crackles with a soft, non-tender abdomen. Laboratory examination revealed a potassium of 6.2 with no EKG changes of hyperkalemia. He was given 30 grams of oral Kayexalate (with sorbitol). Around six hours after ingestion, he started having severe generalized abdominal pain. Physical examination revealed a tense, rigid ab-



domen with rebound tenderness. An abdominal X-ray showed ileus with free subdiaphragmatic air. An emergent laparotomy showed a 1 cm cecal perforation with areas of ischemic necrosis in the terminal ileum. He had a right-sided hemicolectomy and subsequently got hemodialysis. Histopathologic examination showed multifocal ischemic necrosis of the ileum and cecum (Fig. 1) with characteristic rhomboid shaped, basophilic crystals in a mosaic pattern, consistent with Kayexalate (shown by arrow in Fig. 2). [figure1][figure2]



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### Severe Gastrointestinal Bleeding Due to Isolated CMV Enteritis Diagnosed by Double-Balloon Enteroscopy

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**Purpose:** Cytomegalovirus (CMV) primary infection or reactivation can cause serious complications in immunocompromised individuals. However, isolated CMV enteritis in immunocompetent adults is extremely rare. We are reporting a case of recurrent massive gastrointestinal bleeding caused by CMV enteritis in a young female diagnosed by double-balloon enteroscopy (DBE).

**Methods:** Case report.

**Results:** A 38-year-old patient with history of IgA nephropathy on intermittent low-dose steroids (prednisone 5–20 mg/day, 10 days monthly), presented with recurrent massive gastrointestinal bleeding of obscure etiology. Multiple initial endoscopic and radiologic tests including upper and lower endoscopy, push enteroscopy, wireless capsule endoscopy and bleeding scans were negative or non-diagnostic. Urgent upper and lower DBE showed several large semi-circumferential superficial ulcers extending from the proximal jejunum to ileum. Multiple biopsies were positive for CMV by H&E stain and immunohistochemistry. The serum CMV antigen was positive. Despite adequate antiviral therapy, the patient experienced multiple recurrent episodes of massive bleeding, at roughly weekly intervals, requiring a total of 46 units of blood. Ultimately, she underwent an intraoperative DBE which revealed a new jejunal ulcer with active bleeding which was treated surgically. She eventually recovered after prolonged intravenous and oral gancyclovir therapy and was discharged to a temporary rehab facility. This case illustrates several unique features: a severe CMV-related illness in a relatively immunocompetent host; isolated CMV small bowel involvement; recurrent massive bleeding despite adequate antiviral therapy; diagnosis made exclusively by DBE.

**Conclusion:** CMV enteritis should be in the differential diagnosis of patients with massive gastrointestinal bleeding regardless of age or immune competency. DBE may be an extremely useful diagnostic test in patients with massive GI bleeding of obscure etiology.



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**Endoscopic Closure of a Gastrocutaneous Fistula**

Zahid Afzal, MD\*, Ajay Bajaj, MD. *Internal Medicine/Gastroenterology, Advocate Christ Medical Center, Oak Lawn, IL.*

**Purpose:** A 78 year old nursing home patient was seen in consultation for a gastrocutaneous fistula. The patient had a PEG tube that was removed secondary to infection several weeks prior. She subsequently developed a gastrocutaneous fistula. Conservative measures such as high dose proton pump inhibitors and promotility agents to help the fistula heal were unsuccessful. Furthermore, the patient's skin around the abdominal wall had become macerated and exfoliated secondary to frequent leakage of gastric contents.

The patient underwent an EGD. The fistulous opening was well visualized in the gastric body. A single Resolution Clip<sup>R</sup> (Boston Scientific) was applied to close the fistula. Once applied the stomach could be well insufflated. A naso-jejunal tube was then placed endoscopically to maintain the patient's nutrition. Over the next 2 to 3 weeks there was complete healing of the patient's fistula and macerated skin around the PEG site.

Endoscopic closure of gastrocutaneous fistulas has been described in other reports. Our case exemplifies the ease of closure of gastrocutaneous fistulas using endoscopic clips. A single clip was successful in closing the gastrocutaneous fistula in our patient. This is attributed to the larger size of the Resolution Clip<sup>R</sup> and the ability to open and close the clip to ensure optimal positioning before deployment.

The spectrum of endoscopic practice is expanding and there will be novel uses for endoscopic accessories in the future. Many of these new techniques can easily be employed into daily clinical practice by a trained gastroenterologist.

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**Pseudomelanosis Duodeni: An Unusual Rare Finding**

Laura H. Yun, MD\*. *Gastroenterology, University of California San Diego, La Jolla, CA.*

**Purpose:** Melanosis coli or pseudomelanosis coli is a common finding and is a consequence of laxative abuse. Seeing a similar black discoloration of the duodenal mucosa is an unusual, rare finding and called pseudomelanosis duodeni.

A 67 year-old female with a past medical history of CAD, HTN, DM, and chronic renal failure presented with melena. The EGD revealed a few, scattered, nonbleeding antral erosions and an erythematous gastropathy. The mucosa of the first and second portion of the duodenum was noted to have a diffuse, speckled pattern of small black dots which was biopsied. On colonoscopy the mucosa appeared normal, and there was evidence of old blood in the cecum and terminal ileum. Histopathology of the duodenal mucosa revealed black pigment in the macrophages of the lamina propria. These findings were consistent with the diagnosis of pseudomelanosis duodeni.

Pseudomelanosis duodeni is a rare condition first described in 1976 by Bisordi and Kleinman and primarily described in the literature in case reports and case series. It is thought to be a benign condition characterized by the accumulation of dark pigment in the macrophages of the lamina propria. On review of the literature, the majority of the patients are noted to be female and 60 years of age or older. In addition it is associated with certain medical condition such as chronic renal failure, hypertension, gastrointestinal bleeding, and congestive heart failure. It is also associated with the use of certain medications including hydralazine, propranolol, hydrochlorothiazide, furosemide, and iron supplementation. Of note, this patient was female and had chronic renal failure, CAD, and hypertension. She was also on hydralazine, furosemide, and ferrous sulfate.

The exact etiology of the disorder is not known. The pigment is thought to be composed primarily of ferrous sulfide. The proximal duodenum is the site of iron absorption, and it is thought that the iron sulfide complexes are unable to be mobilized and thus accumulate in the macrophages. Other authors have suggested that the pigment is melanin-like because of a similar stain-

ing pattern to actual melanin. They hypothesize that certain substances like furosemide and propranolol contain benzene rings which may be converted to melanin-like pigments via a tyrosinase-like action within the macrophages. Pseudomelanosis duodeni is a rare and interesting finding. There is still no uniform interpretation regarding the nature or source of the pigment. Luckily, the outcome for these patients is good as this is thought to be a benign process.

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**Meckel's Diverticulum Active Bleeding Detected by Capsule Endoscopy**

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**Purpose:** Diagnosing Meckel's diverticulum (MD) before surgery is still a challenge, although the clinical, histopathological and imagiologic features of MD are well known. Several modalities have been proposed for evaluating patients with gastrointestinal hemorrhage from a presumable small bowel source. Even in acute bleeding episodes, repeated diagnostic workups and invasive procedures (angiography, intraoperative enteroscopy) are several times inconclusive.

We present two cases, a 14 and 16 years old patients, admitted to our hospital due to recurrent severe gastrointestinal bleeding (6 gr/dl drops of hemoglobin). Both underwent upper gastrointestinal endoscopy and ileo-colonoscopy, and although no bleeding lesions had been identified, fresh clots were noticed in terminal ileum. Within the first 24 hours of presentation both performed capsule endoscopy (Endocapsule Olympus). In 5 and 6 hours respectively, the bleeding source was identified as an active bleeding oozing from a small diverticulum like orifice in the middle ileum.

Surgical resection of the ileal segment confirmed the presence of the diverticulum with ectopic gastric mucosa. There was no recurrence of bleeding at follow-up after surgery. Both cases illustrate the usefulness of capsule endoscopy availability and its role in investigating acute small bowel bleeding in this age group.

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**Patent Stent 10 Years Post Transjugular Intrahepatic Portosystemic Shunt (TIPS)**

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**Purpose:** TIPS is currently indicated in cirrhotic patients with refractory ascites and recurrent variceal bleeding, not responsive to medical and/or endoscopic therapy. The aim of the procedure is to decrease portal hypertension by creating a permanent tract through the liver parenchyma between the hepatic and portal veins. Common complications include hepatic encephalopathy, shunt dysfunction and occlusion.

**Results:** A 65 year- old male- with history of diabetes, hypertension and chronic alcohol abuse- presented 10 years ago with upper GI bleeding. Work-up at that time, including endoscopy, revealed cirrhosis with actively bleeding esophageal varices. After failed attempts at controlling recurrent UGI bleeding, the patient underwent TIPS in January of 1997. The post-procedure course was unremarkable with no further bleeding episodes or evidence of liver decompensation. The patient remained abstinent from alcohol. A routine Doppler ultrasound performed in January of 2007 confirmed patency of the shunt with normal flow.

**Conclusion:** TIPS is now a well recognized treatment for managing sequelae of symptomatic portal hypertension such as acute or recurrent variceal bleeding, refractory ascites and Budd-Chiari syndrome. Several complications can occur during and after placement of the stent; after hepatic encephalopathy,



the most common one is shunt stenosis/ occlusion. This happens with longer follow-up (52% at 3–9 months and 70% at 9–15 months). Primary patency after TIPS placement has been reported to be 66% after 1 year, and 42% after 2 years. To our knowledge, this case may represent the longest reported graft patency following this procedure.

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# Delayed Colonic Perforation after ESD in a Patient with Ulcerative Colitis

Matthew L. Bechtold, MD, Ajitinder Grewal, MD, Todd W. Kilgore, MD, Srinivas R. Puli, MD, Mainor R. Antillon, MD\*. Division of Gastroenterology, University of Missouri, Columbia, MO.

**Purpose:** Endoscopic submucosal dissection (ESD) removes pre-malignant lesions and intra-mucosal cancers from the GI tract, offering an alternative to surgery. As any procedure, ESD has complications. Certain conditions, such as ulcerative colitis (UC), have not been well-studied with ESD and may lead to increased complications. This case demonstrates a rare incidence of delayed colonic perforation after ESD in a patient with UC.

**Case:** 83 yo male with UC on chronic steroid therapy was found to have a large lateral spreading tumor in the ascending colon on colonoscopy with biopsies revealing no adjacent active UC disease. After the patient refused surgery, he presented for ESD. The 4 × 8 cm mass was identified, raised, and dissected with a conventional needle knife. Two small defects were closed with 7 resolution clips. Post-procedure, IV antibiotics and steroids were initiated and he was admitted to ICU. Lesion revealed a tubulovillous adenoma with underlying cauterized submucosa and no invasive malignancy. On hospital day 3, he improved with softened abdomen and improved leukocytosis. On hospital day 4, he had flatus, decreased abdominal distention and pain, and was extubated. On hospital day 5, he had respiratory distress, increased abdominal distention, and hematochezia. He was emergently re-intubated and underwent exploratory laparotomy. A small opening was noted at the hepatic flexure with bleeding and soilage. A right hemicolectomy with diverting ileostomy was performed. Post-operatively, IV antibiotics and steroids were initiated. Surgical specimen revealed metal clips with full thickness necrosis with associated adjacent hemorrhage, cautery artifact involving the muscularis propria, and acute inflammation with dense inflammatory infiltrate extending to the subserosal fat with focal microabscesses. No cautery artifact was noted in adjacent muscularis propria. The perforation was noted 3.5 cm from the clips. On hospital day 8, the patient was extubated. After a prolonged hospital course, he succumb to sepsis and other co-morbidities.

**Conclusions:** This case demonstrates a rare delayed colonic perforation after ESD in the setting of chronic UC and steroid therapy. Although ESD is an acceptable alternative to surgery, many conditions, such as UC, have not been fully examined. In this case, the delayed perforation may have been secondary to anatomical changes in the colonic wall from UC. More research is required to fully access the safety of ESD in UC.

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# Treatment of Symptomatic Cystic Duct Stone in a Pretransplant Cirrhotic Patient

Timothy M. Saettele, Megan Saettele, Priyanka Tiwari, MD, Matthew L. Bechtold, MD, Srinivas R. Puli, MD, Mainor R. Antillon, MD\*. Division of Gastroenterology, University of Missouri, Columbia, MO.

**Purpose:** Cholelithiasis is prevalent in cirrhotic patients. Laparoscopic cholecystectomy is used to treat symptomatic cholelithiasis but is not recommended for those with cirrhosis. Endoscopic gallbladder stent placement has been described for symptomatic cholelithiasis relief in cirrhotic patients, but is technically difficult or impossible if cystic duct anatomy is not amenable to cannulation. This case demonstrates the placement of a cystic duct stent, stent upsizing, and stone removal in a cirrhotic patient with symptomatic cystic duct cholelithiasis.

**Case:** 44 yo male with cirrhosis (Child-Pugh C), acalculous cholecystitis, and prior cystic duct/gallbladder stent presented with biliary pain. ERCP revealed a 5 mm cystic duct stenosis that could not be traversed and a lack of contrast in the gallbladder. A 10 cm 10-Fr biliary stent was placed into the cystic duct proximal to the stricture. Over the next 22 weeks, two ERCs were performed with the replacement of stents proximal to the stricture. At 22 weeks, ERC revealed the localized stenosis in a tortuous cystic duct and three previous 10-Fr, 8.5-Fr, and 7-Fr stents were removed. A 0.035" Jagwire was passed through the stenosis. A 12 cm 5-Fr biliary stent with pigtails was placed into cystic duct and gallbladder. At 24 weeks, ERC showed the stent in place, a diffuse 20 mm stenosis of the cystic duct, and a possible 8 mm gallbladder stone. At 24–32 weeks, two ERCs were performed with upsizing of the gallbladder stents from 5- to 7-Fr. At 38 weeks, ERC revealed a cystic duct of 6 mm in diameter with a filling defect. A second 15 cm 7-Fr stent with pigtails was placed into the gallbladder. At 44 weeks, ERC showed the two 7-Fr stents which were removed. The cystic duct and gallbladder were swept using a basket and balloon with sludge and stone fragments removed. A choledochoscope was passed into gallbladder over a guidewire and demonstrated clearing of the cystic duct, gallbladder, and CBD by direct visualization. Over time, the patient has remained asymptomatic.

**Conclusions:** This case demonstrates a novel technique effectively used in the treatment of a cystic duct stone in a pretransplant cirrhotic patient. Cystic duct stenting with systematic stent upsizing enabled stone removal without surgery. With this approach, cirrhotic patients that are non-operative candidates may have an endoscopic alternative to allow symptomatic relief.

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# Diagnosis of Mediastinal Tuberculoma with EUS Guided FNA

Alla Grigorian, MD, Houssam Mardini, MD\*, Nicholas Nickl, MD. Division of Digestive Diseases and Nutrition, University of Kentucky, Lexington, KY.

**Purpose:** A 65 year old man presented for evaluation of dysphagia and chest discomfort. Past medical history was significant for diabetes and chronic kidney insufficiency.

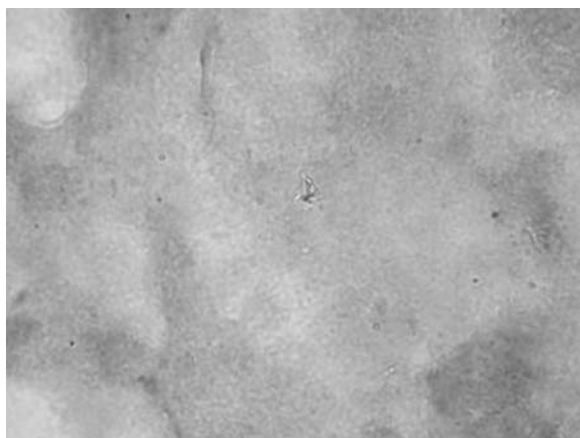
Review of systems and physical examination were not revealing.

Upper GI endoscopy was performed and demonstrated no mucosal abnormality and no obvious endoscopic findings suggestive of pathology that could explain symptoms. Imaging of the chest revealed calcified granuloma in the lower lung fields, small mediastinal lymph nodes, and 5.4 × 2.8 cm hypodense structure adjacent to esophagus with low density center and calcification. Patient was referred to our center for endoscopic ultrasound with fine needle aspiration of above mass.

EUS findings included extrinsic hypoechoic mass/lesion with some calcifications inside noted adjacent to the thoracic esophagus and pericardium. This began from 28 cm from the incisors and extended to 30 cm. Three passes were made with the 22 gauge ultrasound biopsy needle using a transesophageal



approach.[figure1]On site cytology evaluation of the material obtained from the aspirate had a mucoid appearance. Further staining demonstrated a more granular appearance consistent with necrosis. A Fite stain was performed which revealed rare acid fast bacilli.[figure2]Based on above information diagnosis of tuberculoma was made and patient was referred to infectious disease clinic for further investigation and treatment.



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## Post Herpetic Esophageal Neuralgia: A New Entity?

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**Purpose:** Herpes simplex (HSV) esophagitis is frequently seen in immunocompromised patients. It responds to treatment with either acyclovir or valacyclovir. We describe a case of HSV esophagitis with intractable symptoms despite treatment and endoscopic resolution, which responded to an empiric course of gabapentin.

**Results:** A 75 year-old male- post liver transplant for hepatitis C on tacrolimus therapy- presented with progressive odynophagia, dysphagia, atypical chest pain, anorexia and a 25 lb weight loss. He had a history of herpes esophagitis treated one year prior with IV acyclovir followed by valacyclovir for a total of three months. Physical examination was unremarkable. Laboratory studies revealed a normocytic anemia. An esophagogram and chest x-ray were normal. Upper endoscopy showed minimal focal mucosal irregularity of the distal esophagus; biopsies revealed reactive changes with no demonstrable herpetic findings. Viral cultures were negative. Cardiac work-up was normal. The patient was started on a trial of gabapentin 300 mg once daily with a drastic improvement of symptoms. He continues to do well on therapy, at two-month follow-up.

**Conclusion:** Herpes esophagitis is commonly seen in immunocompromised patients. It usually responds well to antiviral therapy. Our patient's symptoms could not be explained by recurrent herpetic esophagitis given paucity of endoscopic findings. The remarkable clinical improvement after initiation of gabapentin therapy raises the possibility of a post-herpetic neuralgia as an underlying etiology. The severity of the clinical presentation and negative history precluded the suspicion of reflux disease as an alternate diagnosis. To our knowledge, this is the first such reported case.

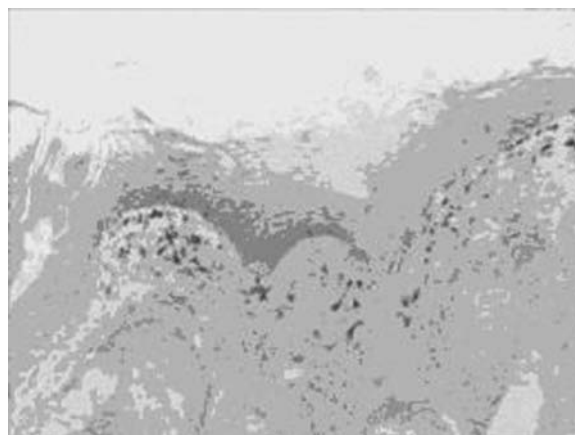
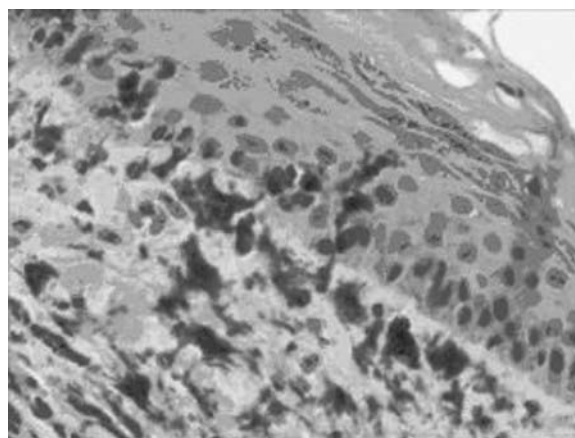
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## Facial Hyperpigmentation in Association with Peginterferon alpha-2a and Ribavirin Treatment for Chronic Hepatitis C Patient: A Case Report

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**Purpose:** Skin hyperpigmentation is a rare complication of interferon based combination therapy for chronic hepatitis C (CHC). Lingual hyperpigmentation is described in the past but facial hyperpigmentation has not been reported. We report an unusual case of facial skin hyperpigmentation in a CHC patient who received therapy with peginterferon alpha-2a and ribavirin. A 45 years old Latino patient was started on a combination therapy with peginterferon alpha -2a and ribavirin for chronic hepatitis C, genotype 1. He responded well with drop in viral load from his baseline 507494 IU/ml to <10 at week 12. Viral load at week 24 was <25. Dark-brown skin pigmentation was noted on his face at week 28. He was referred to a dermatologist for evaluation. A punch skin biopsy showed chronic inflammation with pigmentary alteration and actinic keratosis. Immunohistochemical staining with Fontana Masson stain revealed melanin deposits in the pigmented macrophages. S-100 protein stain showed increased number of melanocytes along basal layer of epidermis (Figs. 1 and 2). Patient successfully achieved SVR. His pigmentation improved slowly but remarkably over 12 months follow up with local hydroquinone gel (4%) and a sun screen.

**Conclusion:** Peginterferon alpha-2a based combination therapy may cause local skin hyperpigmentation which is possibly reversible. Discoloration of the face causes significant concern for obvious cosmetic reasons. Physicians should be aware of potential reversibility of such hyperpigmentation.[figure1][figure2]



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### Ischemic Colitis in a Patient Receiving Carboplatin and Paclitaxel for Non-Small Cell Carcinoma of the Lung

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**Purpose:** We describe a 69-year-old female with a history of metastatic breast cancer and a newly diagnosed non-small cell lung cancer who elected to undergo systemic chemotherapy with carboplatin and paclitaxel. One day after receiving her first cycle of chemotherapy, she presented with nausea, vomiting and hematochezia. She had a normal screening colonoscopy 14 months prior to this event. She had a benign abdomen on examination. Her hemoglobin was normal at the time of admission (13.0 g/dL; normal, 11.5–15.5 g/dL) and remained stable through the course of her hospitalization. Her WBC count was 3600 U/L at the time of admission, with a normal differential. Her laboratories were only otherwise significant for a slight elevation in her transaminases (AST 48 U/L; normal, 15–46 U/L, and ALT 52 U/L; normal 15–46 U/L). Colonoscopic evaluation was performed on the next hospital day and demonstrated hemorrhagic and ulcerated appearing mucosa extending in a segment of approximately 20 cm in the area of the splenic flexure, grossly resembling ischemic colitis. The mucosa proximal and distal to this area appeared endoscopically normal. Pathologic analysis of the biopsy specimens showed changes consistent with a non-specific colitis and suggesting ischemia. Viral and bacterial culture of the specimens demonstrate no growth to date. The patient had a gradually improving course through her hospitalization without any significant intervention, and two weeks subsequent to her discharge she reported that her symptoms had completely resolved.

**Discussion:** Ischemic colitis needs to be strongly considered in the evaluation of hematochezia in the setting of cancer chemotherapy, particularly in patients who have received taxane-based agents. This report will add to a small number of published cases of ischemic colitis associated specifically with taxane-based chemotherapy. Although this outcome was favorable, some published cases have resulted in significant morbidity and mortality. It appears most prudent to hold additional doses of taxane-based therapy, as cases have recurred on rechallenge. Though the precise mechanism remains unclear, direct drug toxicity to the gastrointestinal epithelium is suspected to contribute to this phenomenon. Alternatively, inhibition of angiogenesis could lead to the observed ischemic effect.

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### Endoscopic Hemostasis of Massive Hematochezia after Transrectal Prostate Biopsy: A Case Series

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**Purpose:** Transrectal ultrasound-guided (TRUS) prostate biopsy is the preferred method for diagnosing prostate cancer in the US. Overall, the procedure is safe with a low morbidity and mortality. The incidence of hematochezia after TRUS prostate biopsy varies from 0–37% in published reports. We report our center's experience with endoscopic hemostasis in a series of patients with massive hematochezia after TRUS prostate biopsy.

**Results:** **Case 1:** A 55 y/o man presented with massive hematochezia 12 days after TRUS biopsy. Urgent colonoscopy revealed a visible vessel with adherent clot on the anterior wall of the rectum at the biopsy site. Two hemoclips were successfully placed to control the bleeding.

**Case 2:** A 53 y/o man presented 12 days after TRUS with significant hematochezia. Colonoscopy revealed a clot in the rectum at the biopsy site. A BICAP probe was used to cauterize the bleeding site. No further bleeding occurred.

**Case 3:** A 74 y/o man on aspirin presented with massive hematochezia 5 hours after TRUS biopsy. Sigmoidoscopy revealed an area of arterial spurting

at the biopsy site. The APC was used to cauterize the bleeding site with good hemostasis.

**Case 4:** A 56 y/o man on aspirin and clopidogrel presented with massive hematochezia 1 day after TRUS biopsy. Urgent sigmoidoscopy was performed and arterial spurting was seen at the site of prostate biopsy. The bleeding was controlled with epinephrine injection and BICAP electrocautery.

**Conclusion:** Rectal bleeding is a common complication encountered after TRUS prostate biopsy and is usually managed by local tamponade. Rarely, massive bleeding occurs requiring urgent endoscopy to provide hemostasis. Various endoscopic techniques have been employed including: epinephrine injection, sclerosant injection, electrocautery, band ligation and hemoclip application. Factors predisposing to significant post-procedural hematochezia include the number and location of core biopsies obtained. Patients with internal hemorrhoids are reportedly at increased risk for post-biopsy hematochezia. Both immediate and delayed hematochezia have been reported. Cases 1 and 2 illustrate the unusual occurrence of delayed hematochezia after TRUS biopsy requiring endoscopic hemostasis. Cases 3 and 4 question the reported safety of continued anti-platelet therapy at the time of prostate biopsy. Our series illustrates the important role of endoscopic hemostatic interventions in managing massive hematochezia after TRUS prostate biopsy.

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### Endoscopic Management of Esophageal Varices with Band Ligation in Hepatitis C Patients Receiving Pegylated Interferon/Ribavirin

#### Therapy: Safety and Success of This Approach in Three Patients

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**Purpose:** Hepatitis C (HCV) clearance rates with pegylated interferon/ribavirin are low in patients with cirrhosis. Also, therapy is relatively contraindicated in decompensated disease. Esophageal variceal bleed is a sign of decompensation but many HCV patients on transplant lists bleed from varices or have large varices on screening exams. Therefore, antiviral treatment is being offered to patients with a known history of large varices or variceal bleeding. We report three cases where pegylated interferon/ribavirin therapy was given to patients who were also undergoing endoscopic variceal ligation (EVL). The experience in these patients shows that ligation and antiviral therapy can be undertaken concurrently and may enhance anti-viral therapy outcomes.

**Methods:** Three patients with G1 Hep C and cirrhosis were evaluated at a liver transplant facility. Due to low MELD scores these patients were referred to our local GI practice for another attempt at anti-viral treatment. All had previous unsuccessful interferon/ribavirin therapy. Two patients had previous variceal bleed and the third had large varices on screening EGD. Two patients underwent initial EVL and after variceal eradication was underway anti-viral therapy was started. The third started antiviral therapy without EVL but then elected to undergo prophylactic EVL.

**Results:** These three patients have been on antiviral therapy for 39, 40 and 58 weeks. There have been a total of 10 EVL procedures performed on therapy. The average platelet count of the patients during treatment has been 32K, 44K, and 50K. No episodes of variceal bleed have occurred during or within 72 hours of any EVL procedure. Platelets have not been given before any procedure and treatment has not been interrupted for procedures. One patient had a transient anemia that coincided with black stool but no obvious bleeding occurred. A total of 137 patient-months of antiviral therapy has been given without variceal bleeding. Two patients have achieved late clearance of HCV and the third developed low grade relapse following initial clearance.

**Conclusion:** 1) HCV clearance with pegylated interferon/ribavirin can be achieved in patients who are concurrently undergoing EVL for variceal eradication. 2) EVL appears to be safe and feasible during antiviral therapy. 3) We think that EVL may even enhance outcomes in preventing antiviral treatment cessation/ interruption which may accompany a clinically significant variceal hemorrhage

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**Recurrent Signet-Cell Type Gastric Cancer Simulating Ulcerative Colitis***Matthew Mukherjee, MD, A. Brodsky, MD, Irwin M. Grosman, MD\*. Gastroenterology, Long Island College Hospital, Brooklyn, NY.*

**Purpose:** The patient is a 69 year old man from Ukraine, Russia near the Chernobyl accident. He was evaluated for a six month history of early satiety and weight loss in 2001. He underwent EGD and was found to have three benign gastric polyps, multiple serpentine ulcers and severe erythema and edema in the gastric body. Biopsies revealed poorly differentiated adenocarcinoma, signet ring cell-type. Colonoscopy at that time was unremarkable. Abdominal CT showed a diffuse pattern of infiltration, with a linitis-plastica type appearance. Laparoscopy demonstrated that the tumor was limited to the gastric body and cardia and a total gastrectomy with esophagojejunostomy was performed. Pathology revealed invasive adenocarcinoma with lymphovascular invasion, negative surgical margins and positive lymph nodes – stage IIIb disease. Postoperatively, he received adjuvant chemotherapy with 5-fluorouracil and leukovorin and radiation therapy. He was free from recurrence of the cancer for four and a half years when he returned with left lower quadrant abdominal pain and alternating diarrhea and constipation for several weeks. He underwent colonoscopy which demonstrated inflamed and ulcerated mucosa in the rectum, sigmoid and transverse colon. A preliminary endoscopic diagnosis of ulcerative colitis was made and mesalamine was administered orally and via enema. Stool microbiological studies, ESR, p-ANCA and ASCA were all normal. Endoscopic biopsies revealed mucosal infiltration with signet-ring type cells consistent with metastatic gastric carcinoma in the hepatic flexure, splenic flexure, sigmoid colon and rectum. CT and PET scan showed recurrent disease limited to the colon. He was treated with chemotherapy (5- fluorouracil, Taxotere and cisplatin), which he tolerated well.

**Conclusion:** Gastric adenocarcinoma carries a poor prognosis partly because symptoms often develop after the disease has become locally advanced or metastatic. The most common sites of metastasis are liver, lung, peritoneum and bone marrow. Less common sites include umbilicus (“Sister Mary-Joseph’s nodule”), ovary (“Krukenberg tumor”), rectum (“Blumer’s shelf”), kidney, bladder, brain, heart and thyroid. The colon has been described in several case reports as a site of local spread (transverse colon) or distant metastasis. Recurrent gastric cancer presenting as inflammatory bowel disease is very rare, with only one other previous case reported in the literature.

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**Acute Hemorrhagic Colitis in 25 Year Old Man Treated for Flu like Symptoms***Dana M. Kaplan, Jianlin Xie, MD, PhD, Anisha Thadani, MD, Sita Chokhavatia, MD\*. Gastroenterology, The Mount Sinai Medical Center, New York, NY.*

**Purpose:** A 25-year-old previously healthy male developed nausea, non bloody vomiting, fever with chills, muscle aches and watery diarrhea. He was treated for influenza B in an emergency room the next morning with a 5 day course of a neuraminidase inhibitor – oseltamivir plus other symptomatic treatment. That evening he noted onset of left lower quadrant abdominal pain, cramping and sharp in nature, progressively increasing in intensity over the next 3 days which was accompanied by an increased frequency of bloody bowel movements (15 bowel movements of small quantity- “couple of teaspoons”) and presented to our hospital. No recent travels, sick contacts or prior antibiotics use were reported; no family history of IBD. On examination he was not in acute distress; had stable vitals and was afebrile; abdomen exam revealed normal bowel sounds, soft but tender in the left lower quadrant; no stool in vault but Guaiac positive on rectal exam, no hemorrhoids or fissures. Stool was negative for WBC and O/P; stool cultures were negative and Clostridium difficile toxins also negative. Thick-

ening of the bowel wall from distal descending to the proximal sigmoid colon was seen on CT. In addition to intravenous fluids, metronidazole and ciprofloxacin were started for presumed infectious colitis. Patient had discontinued oseltamivir after 2 doses. Sigmoidoscopic examination revealed a severely inflamed, edematous, and erythematous mucosa from the anal verge to 40 cm and sparing of the rectal mucosa. Biopsies from the hemorrhagic sigmoid and normal appearing rectum revealed mildly active chronic colitis suggestive of ischemic/concomitant infectious colitis and normal rectal mucosa, respectively. The patient’s symptoms began to improve after halting oseltamivir treatment. Metronidazole was discontinued after 2 day treatment but he completed a 5-day ciprofloxacin course. Diarrhea significantly improved with decreased frequency and minimal bright red blood per rectum. His symptoms resolved completely and he was discharged on hospital day 4 (9 days after initial onset of symptoms).

Acuity and short duration of symptoms were suspected secondary to infectious and/or ischemic colitis. However, acute hemorrhagic colitis induced/exacerbated by oseltamivir could not be ruled out since the symptoms worsened following its administration and improved upon discontinuation. Acute hemorrhagic colitis induced by oseltamivir was first reported by a Japanese group in 2006.

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**Isolated Gastric Malakoplakia Associated with Helicobacter Pylori Infection: A Case Report and Review of Literature***Shoba Mendu, MD, Michael Piper, MD\*, Ved Singla, MD. Gastroenterology, St. John Providence Hospital, Southfield, MI.*

**Purpose:** Malakoplakia is a rare chronic inflammatory disorder characterized by a mass like accumulation of histiocytes and pathognomonic intracellular and extracellular siderocalcific inclusion bodies called Michaelis-Gutmann bodies. It most frequently involves the genitourinary tract. Involvement of gastrointestinal tract, lymph nodes, brain, bone, lungs, adrenal glands and skin has also been reported. Isolated gastric malakoplakia is extremely rare. Here we report a case of isolated gastric malakoplakia associated with Helicobacter pylori (H pylori) infection with complete histologic and symptomatic resolution after treatment.

**Methods:** A 71-year-old African American man presented with dyspepsia, epigastric discomfort, diarrhea and weight loss of more than one year duration. There was no clinical evidence of immunodeficiency or malignancy. Upper gastrointestinal endoscopy revealed mild inflammation with scattered white plaques in the gastric antrum and body with a 5 mm polyp in the body. Examination of the biopsy of the plaques revealed lamina propria replaced by regular, small, round nuclei with eosinophilic cytoplasm containing Michaelis-Gutmann bodies diagnostic of gastric malakoplakia. A moderate number of H pylori like organisms were seen on Warthin Starry stain. Colonoscopy revealed one cecal and one descending colon tubular adenoma. There was no evidence of malakoplakia or malignancy seen elsewhere. He was treated with lansoprazole, amoxicillin and clarithromycin for ten days and his symptoms resolved. Repeat gastroscopy after 4 months showed no evidence of malakoplakia or H pylori organisms.

**Results:** Reports of isolated gastric malakoplakia are few in number. Malakoplakia is associated with concomitant diseases such as leukemia, lymphoma, alpha chain disease, immunodeficiency, miliary tuberculosis, villous adenoma and carcinoma. Infectious agents have been implicated as the cause of malakoplakia in the majority of cases. To our knowledge this is the first case reported showing an association with H pylori infection with complete symptomatic and histologic resolution after treatment. Since malakoplakia mimics malignancy and can be associated with colorectal carcinoma in 30% of the cases, a thorough evaluation is essential

**Conclusion:** Isolated gastric malakoplakia is extremely rare. Diagnosis and treatment of predisposing conditions is very important to prevent complications.

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### Clinical Utility of Adjunctive Naturopathic Products To Improve the Tolerability of Interferon Based Regimens for Hepatitis B and C: A Report on Four Patients

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**Purpose:** To observe any clinical utility of adjunctive naturopathic products like Milk thistle, turmeric, Siberian Ginseng, Schisandra and Bupleurum in improving the tolerability of standard Interferon based therapies for Hepatitis C and B patients.

**Methods:** 3 patients with hepatitis C on standard pegylated interferon alpha-2b and ribavirin and 1 patient with hepatitis B on pegylated interferon alpha-2a were instructed to simultaneously take two 220 mg capsules of Milk Thistle, 1000 mg of turmeric capsules, 1000 mg of Siberian Ginseng, 3 cups tea daily with 1 tsp each of schisandra and bupleurum tinctures respectively for the initial 2 months. They were assessed every 2 weeks for the side effect profiles including fatigue, energy loss, myalgias, mood swings and flu like symptoms. Their lab parameters were analysed and the subjective tolerability of therapy was also graded from 1(Intolerable) to 5(Very Tolerable).

**Results:** All four patients receiving the above naturopathic supplements did not report any serious subjective side effects warranting any dose reduction or stoppage of standard therapy. They maintained their normal routines without any fatigue or energy loss. All reported tolerability scores of 3 or higher. The patients also felt that the natural supplements seemed to help them subjectively, with no adverse sequelae. The CBC profiles were also maintained in acceptable ranges and did not warrant any dose reductions of the standard therapy.

**Conclusion:** The tolerability profiles of the four patients receiving naturopathic supplements with the standard Hepatitis B and C interferon based therapies was very good, with none of the patients requiring dose reductions or stoppage of standard therapy. The patients also reported a feeling of subjective well-being. Whether this could be related to a non-specific immuno-booster effect or a placebo phenomenon, naturopathic supplements appear to have a clinical role in improving the patient tolerability of interferon based hepatitis regimens. Further large scale standardized controlled studies are needed to assess the clinical utility of these unregulated "food supplements".

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### Gastric Cancer Recurrence in Small Bowel after Subtotal Gastrectomy with Billroth II Gastrojejunostomy

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**Purpose:** A seventy-nine year old Caucasian male with gastric adenocarcinoma (T2aN1M0) who underwent subtotal gastrectomy with Billroth II gastrojejunostomy and chemotherapy three years ago was referred by his oncologist for a nine pound weight loss over one month. An esophagogastroduodenoscopy was performed and a five centimeter friable mass was identified in the efferent loop five centimeters distal to the gastrojejunostomy. A biopsy of the mass revealed moderately to poorly differentiated adenocarcinoma. Exploratory laparotomy revealed the tumor in the efferent loop which was excised and a second suspicious area of small bowel was resected. The pathology for both small bowel segments were infiltrating moderately to poorly differentiated adenocarcinomas. The pathology from the small bowel was compared with the pathology of the original gastric adenocarcinoma from three years ago and were identical. The patient therefore had recurrence of his gastric cancer in his efferent limb in two separate locations three years after his surgery.

Locoregional recurrence of gastric cancer is most commonly found in the gastric stump. There have been rare reports of gastric cancer recurrence in the J-pouch and in the efferent loop. These cases were reported in patients from the Far East, where incidence of gastric cancer and gastric cancer recurrence

is higher and surveillance is more extensive. However this is the only reported case of recurrence in the efferent limb at two separate sites. This is also the first reported case in North America of gastric cancer recurrence in the small bowel.

There is no universal consensus for surveillance following curative surgical resection for gastric cancer. Prognosis for recurrent disease remains poor, yet there are no guidelines to help detect recurrence at an earlier and more treatable stage. We propose yearly surveillance with esophagogastroduodenoscopy in patients with gastric cancer resection.

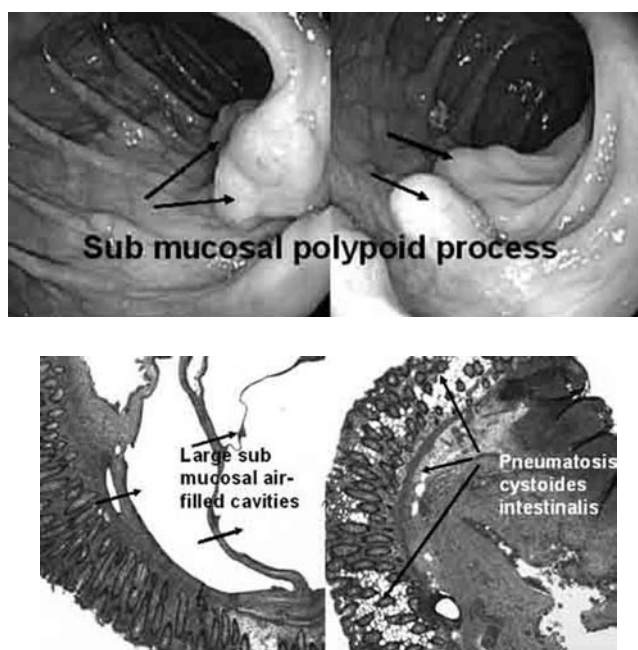
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### Pneumatosis Intestinalis. The Question Is To Be or Not To Be – A Polyp!

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**Purpose:** 57 year old male with history of diabetes and hyperlipidemia presented with abdominal distension and flatulence of several months duration. Initial colonoscopy by the referring gastroenterologist revealed multiple large, broad based, transverse colon polyps. Snare polypectomy was deferred due to concerns regarding diagnosis and potential complications. Laparoscopic resection vs. endoscopic resection by a skilled endoscopist was discussed with the patient who opted for the latter. Colonoscopy performed at our institution revealed many 5–25 mm, sub-mucosal lesions. The morphology was that of a distinct raised globular lesion or a confluent multilobulated mass (Fig. 1). The endoscopic impression was pneumatosis coli. The largest polyp was partially snared to remove the mucosa and well biopsies were taken to get deeper tissue. Biopsies revealed numerous gas filled cysts in mucosa and sub mucosa, lined by epithelioid histiocytes (Fig. 2).

Pneumatosis intestinalis is characterized by multiple gas-filled intamural cysts in the small or large bowel. It may be primary or secondary due to peptic ulcers, IBD, feeding jejunostomy, ruptured diverticuli, clostridium difficile, AIDS enterocolitides, COPD, mechanical ventilation, post endoscopy and intestinal ischemia. This finding may be incidental on endoscopy or routine imaging. Symptomatic patients may present with diarrhea, hematochezia, abdominal pain, distension or flatulence. Hyperbaric oxygen treatment and



antibiotics are helpful in some instances. However, in cases of intestinal ischemia and perforation, pneumatosis is an ominous sign and emergent surgery is indicated.

**Conclusion:** Our patient had persistent irritable bowel symptoms likely unrelated to pneumatosis. Endoscopic recognition and confirmatory biopsies avoided an unnecessary surgical resection, for an otherwise benign condition.[figure1][figure2]

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### MALTOMA of the Colon Presenting as Autoimmune Hemolytic Anemia

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**Purpose:** Gastrointestinal causes of anemia include blood loss, nutritional deficiency, malabsorption of nutrients, hypersplenism, or drug induced bone marrow suppression or hemolysis. Autoimmune hemolytic anemia is a rare manifestation of GI disease; when it occurs, consider gastrointestinal lymphoma.

**Objective:** We report a case of MALTOMA of the colon presenting as autoimmune hemolytic anemia (first report).

**Case Report:** A 60 year old man presented with worsening exercise intolerance and dizziness for three months and without weight loss, fever, night sweats or GI symptoms. *Examination:* icterus, otherwise unremarkable. *Investigations:* Hemoglobin: 7.2 g/dl, reticulocyte count: 17.22%, haptoglobin 22 mg/dl, unconjugated bilirubin 2.6 mg/dl, LDH 644 U/L; Direct antiglobulin test: weakly positive; Bone marrow biopsy: erythroid hyperplasia (M: E = 0.3:1); thus confirming a diagnosis of **autoimmune hemolytic anemia**. *Treatment:* PRBC transfusions and prednisone. *Evaluation of underlying etiology:* CT abdomen (Fig. 1): a large mass transverse colon (arrow); Colonoscopy with high frequency ultrasound probe sonography: a large sub-mucosal mass in the mid transverse colon. *Surgery:* Laparoscopic transverse colon resection. *Pathology (Fig. 2):* small lymphocytic lymphoma, with immunohistologic features consistent with **MALT lymphoma of colon**. *Course:* Patient recovered fully and is currently on prednisone; last hemoglobin: 11.7 g/dl.

**Conclusions:** Our case demonstrates that value of investigation of underlying cause of autoimmune hemolytic anemia. The underlying problem is **MALT lymphoma of the colon without gastrointestinal symptoms**.

**Literature Search:** We did not encounter a case of MALT lymphoma of the colon with autoimmune hemolytic anemia in the literature. [figure1][figure2]

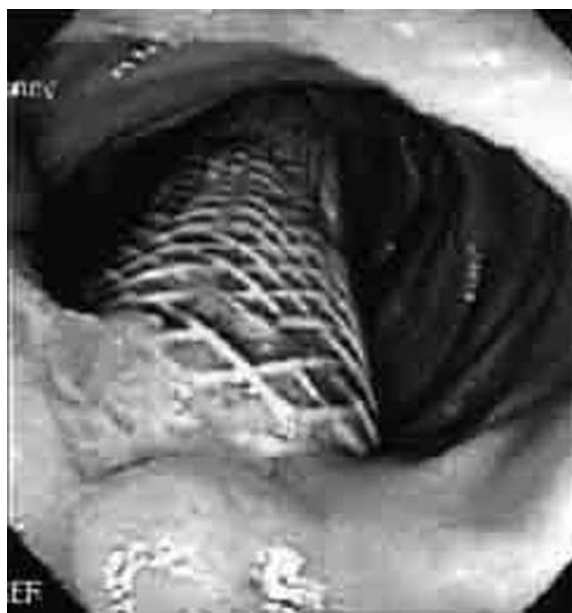


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### Retrieval of Distally Migrated Esophageal Stent Using Enteroscopy

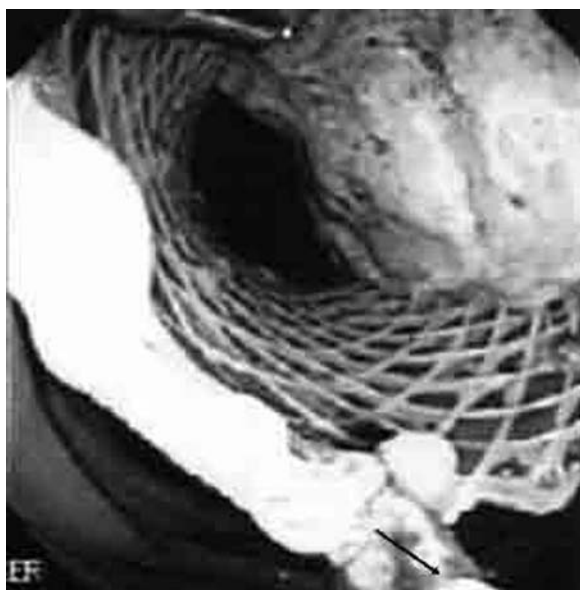
Raja S. Vadlamudi, MD, Mark F. Young, MD\*. Department of Internal Medicine, East Tennessee State University, Johnson City, TN.

**Purpose:** Migration of esophageal stent is an important complication (6% to 18%). Stent migrations are usually treated with conservative measures. We present a case where the displaced stent is removed using enteroscopy.



**Case Report:** A 48 year old male smoker with intermittent dysphagia to solids and heartburn underwent esophagogastroduodenoscopy (EGD) with biopsy which showed squamous cell carcinoma of the distal esophagus confirmed by pathology. Exploratory laparotomy showed metastatic involvement of the celiac lymph nodes. He underwent chemotherapy and radiation therapy without any complications. Later esophagectomy with splenectomy was done for worsening dysphagia. He developed an esophageal anastomotic leak postoperatively. An esophageal deficit of 1.5 cm was identified on EGD and was reduced using surgical clips. A silicone coated polyflex esophageal stent was also placed at the anastomotic site. Few days before the proposed stent removal, he developed abdominal discomfort. The abdominal x-rays showed possible distal migration of the stent in to the left upper quadrant of the abdomen. He underwent enteroscopy and the stent, initially found in the jejunum, was pulled into third part of the duodenum (Fig. 1). For lack of facility to use forceps with enteroscope, a pediatric colonoscope was used to remove the stent using rat toothed forceps (Fig. 2). Neither small bowel defects nor distal esophageal deficits were noted on repeat enteroscopy.

**Conclusions:** This case illustrates the retrieval of distally migrated esophageal stent using enteroscopy with no untoward effects or complications. [figure1][figure2]



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#### Metastatic Melanoma in a Dialysis Patient with Vomiting Diagnosed by Gastric Polyp Biopsy

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**Purpose:** Gastric polyps are a common incidental finding on upper endoscopy. Although the majority of these polyps are benign, rarely they represent primary gastric malignancy, lymphoma or even metastatic disease. We describe a case of metastatic melanoma without a primary cutaneous lesion diagnosed by endoscopic biopsy of a gastric polyp.

**Case Summary:** A sixty-three year old Irish female with past medical history significant for coronary artery disease, hypertension and end stage renal disease requiring dialysis presented with complaints of intermittent vomiting for two weeks. Her vomiting was not associated with food and she denied nausea, retching, weight loss, hematemesis or melena. Physical examination including a thorough neurologic, ophthalmic and dermatologic exam was performed which was normal. Comprehensive metabolic panel and complete blood count were within normal limits. An upper endoscopy

was performed which revealed multiple 5 mm polyps in the body of the stomach. Histology of the polyps revealed that they were malignant and special stains were positive for vimentin, HMB45, S100, Melan A, and CEA consistent with metastatic melanoma. Computerized tomography (CT) of the chest/abdomen and pelvis were within normal limits. CT of the brain revealed calcified/hemorrhagic lesions consistent with metastatic disease.

**Conclusion:** Gastric polyps are a common finding on upper endoscopy occurring in 2.5% of cases, most of which are hyperplastic. Metastatic disease to the stomach is rare, but has been described with breast cancer, renal cell carcinoma and melanoma. Metastatic melanoma is usually from the skin but, can be secondary to non-cutaneous lesions such as those of ocular and mucosal origin. Primary gastric melanoma has been reported but usually is seen as a large ulcerated mass. In our case no primary lesion could be identified likely, secondary to regression of a primary cutaneous lesion as occurs in 2% of melanoma cases. Our case highlights that although most gastric polyps are benign, gastric cancer and metastatic disease must always be entertained and biopsy should be considered.

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#### Ciprofloxacin-Induced Acute Cholestatic Liver Injury and Associated Renal Failure from Acute Tubular Necrosis

Amy J. DiChiara, MD, Matt Atkinson, MD, Kenneth E. Sherman, MD\*. Department of Internal Medicine, University of Cincinnati, Cincinnati, OH.

**Purpose:** Ciprofloxacin, a fluoroquinolone antibiotic commonly prescribed for a variety of infections has generally been well-tolerated; however, there are rare reports of it causing hepatic failure or renal failure. In this case report, we describe a 65 year-old man with a history of ischemic cardiomyopathy and mild renal insufficiency (baseline creatinine 1.2–1.3), who developed acute cholestatic jaundice and acute renal failure following treatment with ciprofloxacin 500 mg two times a day for cellulitis. Six days into his treatment course, routine labs showed the following: AST: 319, ALT: 157, AP: 711, bilirubin: 8.5, BUN: 36, creatinine: 2.3, INR: 6.6. The patient had no history of previous liver disease, alcohol, recent new medications, nor other toxic/herbal exposure. Total and direct bilirubin eventually rose to 25.3 and 15.6, while AST, ALT, and AP improved to 139, 102, and 226, respectively. Liver biopsy revealed prominent canalicular and intrahepatocyte cholestasis as well as focal hepatocyte ballooning with surrounding neutrophils and lymphocytes, but no significant necrosis. Other causes of liver injury were ruled out. Simultaneously, the patient became oliguric, creatinine continued to rise, and eventually required regular hemodialysis. Kidney biopsy revealed acute tubular necrosis (ATN). Within two months of stopping the ciprofloxacin, the patient was off dialysis and back to his baseline creatinine in three months. Liver tests normalized by five months.

**Discussion:** There are 15 reported cases of ciprofloxacin-induced hepatotoxicity. The time course between initiation of ciprofloxacin and development of cholestatic liver injury as well as the improvement of this injury with the removal of the offending agent strongly suggested ciprofloxacin as the cause of the liver injury. Additionally, the time course and severity of renal failure suggested ciprofloxacin-induced ATN as the cause of the renal failure. There are several reports of ciprofloxacin-induced acute renal failure secondary to interstitial nephritis; however, there has been only a single case report of ATN from ciprofloxacin. To our knowledge, this represents the first case report of simultaneous acute cholestatic liver injury and ATN secondary to ciprofloxacin.

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#### Elevated Alfa Fetoprotein: Looking beyond Hepatocellular Carcinoma

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**Purpose:** Carcinoid tumors are the tumors of neuroendocrine system comprising 1–2% of all gastrointestinal malignancies. Primary hepatic carcinoid



is a very rare tumor. Less than 70 cases in English literature are reported so far. We report on a patient who developed primary hepatic carcinoid tumor in a non cirrhotic liver with elevated fetoprotein which is a rare association. 54 yr old male presented with six month history of bloating and gaseous sensation, dull right upper quadrant nonradiating pain 3/10, decreased appetite, weight loss of 20 lbs over 6 month period, distant history of Hepatitis A, >40 pack year smoking history, without history of alcohol or illicit drug use. Physical exam revealed non tender hepatomegaly otherwise unremarkable. CT scan of abdomen showed markedly enlarged liver with multiple masses. Labs showed CBC and BMP to be normal, total Bilirubin 1.2, ceruloplasmin 45, Iron 45, HepB core antibody reactive, Hep B surface antigen and antibody non reactive, Hep C antibody non reactive, AST 151, ALT 51, Alkaline phosphate 262, Amylase 92, Lipase 561, Alfa fetoprotein 10313.3, CEA 4.3. Histopathological examination revealed highly cellular smears with groups of tumor cells demonstrating high nuclear to cytoplasmic ratios, numerous mitotic figures, granular chromatin, no visible nucleoli and a vague rosette-like pattern. Immunohistochemistry was positive for chromogranin and synaptophysin and negative for cytokeratin 7 and 20. Serial Octreotide scan showed mild non-homogenous uptake in the left lobe of the liver and were inconclusive for metastatic carcinoid.

Patient was transferred to Tertiary hospital and was given 6 cycles of chemotherapy Carboplatin + Etoposide due to extensive liver involvement and presence of small cells. He achieved partial response without development of new lesions on the most recent follow up CT scan of abdomen and pelvis.

**Conclusion:** Diagnosis of primary hepatic carcinoid is difficult because of its rarity and histological similarity to hepato cellular carcinoma. Misdiagnosis is easy especially with elevation of alpha fetoprotein. Liver masses with AFP level higher than 4000 are usually treated as HCC, even in Hep B neg patients. Thus, the diagnosis of HCC should be confirmed with biopsy especially in liver masses presenting with elevated AFP and negative Hep B serology.

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# **A Late Presentation of Blue Rubber Bleb Nevus Syndrome Diagnosed by Laparoscopic-Assisted Double Balloon Enteroscopy**

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**Purpose:** A 78 year-old man with peptic ulcer disease and new atrial fibrillation requiring warfarin presented with weakness and anemia at an outside institution. Initial EGD and colonoscopy found no bleeding source. A tagged RBC scan showed a left upper quadrant blush. An arteriogram had no arterial or venous abnormalities. Push enteroscopy identified nonbleeding dilated venous structures in the proximal small bowel. Video capsule endoscopy found round, blue lesions in proximal small bowel, red blood in mid-distal jejunum, and black fluid obscured the distal small bowel. He was transferred to our institution for double balloon enteroscopy (DBE). On physical exam, he had a 2 mm lower lip purple papule and a 4 mm purple papule on his scrotum. His stool was brown but hemoccult positive. External exam of the bowel with laparoscopic-assisted DBE identified blue lesions on small bowel and colonic serosal surfaces. Endoscopically, flat prominent veins were noted in the distal esophagus and gastric antrum, blue polypoid lesions were identified in the small bowel with relative ileal sparing, and red blood with clot was found in the mid-jejunum. Despite vigorous warm water washes, no active bleeding lesion was identified to warrant endoscopic or surgical intervention. Blue Rubber Bleb Nevus Syndrome (BRBNS) was diagnosed based on characteristic cutaneous venous malformations and associated visceral lesions. Given late age of presentation, bleeding provoked by anticoagulation, and extent of bowel involvement, he has been treated conservatively with octreotide without a subsequent bleed for 8 months.

BRBNS is a rare disorder in which cutaneous lesions, often present in early childhood, tend to be multiple, blue, compressible lesions that rarely bleed unless traumatized. In contrast, GI lesions, usually evident in early adulthood, extend from the oral cavity to anus with easy bleeding. Conservative medical management has been reported using corticosteroids, interferon, octreotide,

and iron supplements. Endoscopic therapy has included sclerotherapy, band ligation, laser photocoagulation, and polypectomy. Most recently, a combination of radical endoscopic and surgical local excision of lesions has been reported to be successful and sparing of extensive bowel resections. To our knowledge, this is the first use of DBE in the diagnosis and management of BRBNS deep in the small bowel. With the first bleeding episode at age 78, it is also one of the latest presentations of BRBNS ever diagnosed.

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# **Massive Upper GI Bleed Secondary to Splenic Artery Pseudoaneurysm**

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**Purpose:** 22 year old male, history of abdominal trauma, presented with sudden onset of 3 episodes of hematemesis associated with abdominal pain and loss of consciousness. He denied previous episodes of GI bleeding. Two years prior, he had multiple stab wounds to the abdomen and subsequently underwent exploratory laparotomy and ostomy with reversal for perforated bowel. Reports heavy alcohol use on weekends and smokes 1 ppd  $\times$  6 years. Upon arrival to the emergency room, vital signs were stable: P73, BP 122/68 with no orthostasis. Abd exam: + BS, NT, ND, + midline and ostomy scars, no organomegaly. Rectal exam: brown stool, guaiac positive. NG lavage was not performed. Labs: WBC 11,900 mm<sup>3</sup>, Hg 12.5 g/dL, Hct 37.9%, Platelets 323/mm<sup>3</sup>, BUN/cr ratio 19 with normal coagulation profile and liver tests. An EGD was performed. A large fresh clot was seen in the gastric body which could not be suctioned. In addition, fresh blood was seen in the second portion of the duodenum, but no source of bleeding was identified. During endoscopy, the patient had several more episodes of hematemesis and was taken to interventional radiology. A 5 F catheter was placed in the celiac axis and an angiogram was performed. A pseudoaneurysm off the mid splenic artery was identified as the source of bleeding and coils were deployed and packed into the pseudoaneurysm. Repeat angiogram showed no residual flow with good thrombosis. Subsequently, the patient was discharged with no further episodes of GI bleeding and Hct 35%. Few cases have reported GI bleeding in patients where pseudoaneurysms have been thought to spontaneously erode into the GI tract secondary to compression/stress/trauma. Since this patient had sustained prior abdominal trauma in the same anatomical location as the formation of the splenic artery pseudoaneurysm, spontaneous fistularization of the pseudoaneurysm and the gastric wall could have occurred thus explaining his presentation. A thorough review of the literature has reported pseudocyst and pseudoaneurysm fistularization to arteries supplying the GI tract or to the pancreatic duct in patients with chronic pancreatitis resulting in upper GI bleeding. However, to date, there is no reported case of a pseudoaneurysm of the splenic artery caused as a result of prior abdominal and presenting as trauma hematemesis. Hence, as gastroenterologists, we must be aware of the increasing role of angiographical methods for diagnosing and controlling acute GI bleeding.

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# **Fever and Sepsis as an Unusual Complication of Erosion of an IVC Filter into the Duodenum**

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**Purpose:** Erosion of an inferior vena cava (IVC) filter into the GI tract is rare. Similarly, fever and sepsis is an underappreciated complication of intravascular device migration. We report a patient with an unexpected duodenal-caval fistula detected endoscopically as the postulated cause of unexplained recurrent sepsis.

**Case Report:** A 67-year-old presented with one week of confusion. He denied abdominal complaints. He had been discharged 2 weeks earlier with *Klebsiella pneumoniae* sepsis. Past medical history was significant for



multiple pulmonary emboli with placement of a non-retrievable IVC filter 2 years previously. Two months prior to the current admission, UGI endoscopy for Barrett's esophagitis screening lead to the seemingly incidental discovery of a thin, metallic foreign body protruding into the duodenum. On exam, temp. = 101.6°F, blood pressure = 140/80 without postural change, pulse = 74/min. Cardiac, pulmonary and abdominal exams were normal. WBC count = 16,000; 4 out of 4 blood cultures were positive for *Staphylococcus aureus*.

Progressive dysphagia due to Parkinson's disease required percutaneous endoscopic gastrostomy tube placement. At UGI endoscopy, a thin metal wire was protruding through the wall of the second portion of the duodenum. A clean-based, non-bleeding ulcer was on the opposite wall. The finding was consistent with migration or erosion of a non-retrievable IVC filter through the duodenal wall. CT scan confirmed this finding. He declined further treatment.

**Discussion:** Perforation of an IVC filter into the GI tract is rare. Other potential mechanisms of IVC-duodenal fistula are penetrating injury; erosion of tumor, abscess or pseudocyst. Clinical manifestations of filter migration into the duodenum are diverse, including chronic abdominal pain, GI bleeding of any magnitude, fever or sepsis. Clinical signs of infection, such as confusion in our patient, may be non-specific and misleading, mimicking more common disorders. Delay in diagnosis is common. We postulate that duodenal ulceration and sepsis were complications of an IVC filter. Fever and bacteremia are rare, reported complications of duodenal migration or perforation of these devices. Filter erosion should be considered in any patient with a history of filter placement and unexplained chronic abdominal pain, GI bleeding, fever or sepsis.

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### Recurrent Hematochezia – A Rare Presentation of the Klippel-Trenaunay-Weber Syndrome

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**Purpose:** A 27 year old male presents with 8–10 episodes of painless hematochezia per month over the past 9 years. Physical examination revealed hypertrophy and large varicose veins in the right thigh. PMHx was significant for a port-wine stain on his right thigh early in childhood. At age 8, he developed oozing of his right thigh and underwent laser therapy. At age 12 he noted a “bumpy” consistency of his right thigh and underwent a right leg venectomy. Pathology revealed arteriovenous malformations (AVMs). His first episode of hematochezia occurred at age 18; work-up at that time included normal EGD, colonoscopy, and capsule endoscopy. Our repeat colonoscopy showed grade 1 internal hemorrhoids and prominent rectal veins to 10 cm from the anal verge. CT scan showed calcified phleboliths in the peri-rectal fat relating to multiple dilated venous structures. MRI/MRV of the pelvis showed an enlarged fetal lateral limb-bud vein extending into the right lateral thigh, enlarged peri-rectal veins and hemangiomatosis. Right leg venogram revealed extensive venous collaterals and an aberrant sciatic vein extending from the right lateral thigh. Additionally a direct communication from the common femoral vein and deep system to the large venous collaterals in the knee and thigh was noted. These findings prompted a diagnosis of Klippel-Trenaunay-Weber Syndrome (KTWS). He then underwent endovenous ablation of his right sciatic vein and a large collateral vein, followed by U/S-guided sclerotherapy with foam injection. Follow-up flexible sigmoidoscopy revealed near complete ablation of rectal varices 6 months from first presentation. There have been no further episodes of hematochezia. KTWS is a sporadic congenital anomaly characterized by the presence of a port-wine stain, varicose veins, hypertrophy of bony/soft tissues and AVMs. Rectal bleeding is a rare complication of KTWS and there have been few reported cases of hematochezia secondary to rectal varices from KTWS. The

diagnosis is supported by histologic demonstration of AVMs. Treatment options include debulking, radiotherapy, sclerotherapy or surgery. This case illustrates the importance of endoscopic recognition of rectal varices as it may unmask manifestations of a severe underlying systemic disorder.

## 621

### An Unusual Cause of an Abdominal Mass

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**Purpose:** A 29 year old white male had been having worsening abdominal pain and distention over two months. During this time he had nausea, early satiety, and night sweats. He had noticed a painful mass near his epigastrium. He had not had any weight loss, jaundice, or change in bowel pattern. On physical exam he had a firm, distended abdomen with normal bowel sounds and a large mass extending from the epigastrium to his pelvis. A CT of abdomen was obtained that showed a large 27 cm mass in diameter arising from the retroperitoneum, involving the liver, and extending to the pelvis. There were multiple omental and liver metastases along with extensive retroperitoneal lymphadenopathy. A needle biopsy was performed that was consistent with Ewing sarcoma. The patient was treated with vincristine, doxorubicin, cyclophosphamide and actinomycin D. Surgery was not an option due to extensive metastases.

Ewing sarcoma is a neuroectodermal tumor of the bone that may metastasize to other bones and lungs, and very rarely spreads to other organs. It is usually found in children, with average age at diagnosis of 10–20 and an incidence of 1 per 3.3 million. Extra-osseous Ewing sarcoma is rare and has been described in the retroperitoneal cavity, stomach, gallbladder and small bowel. Retroperitoneal origin of the cancer is rare only 15 cases have been reported worldwide. Adverse predictors for survival are metastatic disease at presentation, primary extraosseous tumor, or age older than 26. He is currently undergoing a second regimen of chemotherapy with ifosfamide and etoposide, due to poor response with first chemotherapy regimen.

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### Isolated Cecal Infarction with the Radiological Picture of a Mass Lesion in a Patient with an Acute Abdomen and No Obvious Predisposing Factors

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**Purpose:** Isolated cecal infarction is an *uncommon* entity, which can be due to vasculocclusive or nonocclusive causes. Here we present a case of a healthy elderly female with abdominal pain who was found to have an *isolated cecal gangrene*.

An 82 year old Caucasian female presented to the emergency room with the acute onset of right lower quadrant abdominal pain. Her medical history was pertinent only for well-controlled hypertension and a surgical history of a left breast lumpectomy. At the time of admission, the patient was febrile with no hemodynamic instability; lab values revealed only leukocytosis (WBC 13,800/mm with 90% neutrophils). Computed tomography-intended to rule out appendicitis- revealed focal wall thickening of the cecum and ascending colon suggestive of a cecal mass (Fig. 1). Colonoscopy was not recommended because of the possibility of perforation. Due to the clinical picture and CT scan findings of a possible cecal mass, the patient underwent exploratory surgery. Intraoperatively, gangrene isolated to the cecum with full thickness necrosis was found. No free perforation was noted. Mesenteric pulses were palpable. The patient underwent right hemi-colectomy and had an uneventful postoperative course.

Histopathology revealed severe ischemia of the cecum with *transmural infarction* of the *cecal wall* and acute peritonitis of the cecal serosa. Proximal (*ileal*) and distal (*colonic*) resection margins and appendix showed *no evidence of ischemia*. The cecal vessels showed no atherosclerosis as well as no evidence of vascular occlusion or vasculitis. Work-up with cardiac

echocardiography revealed no focus of embolic disease. The patient was discharged in stable condition one week after surgery.

To our knowledge, this is a unique case report of *isolated cecal gangrene* in a patient with *no predisposing cause*. Isolated cecal gangrene may present as a diagnostic dilemma owing to its *uncommon* occurrence and *atypical* presentation-in this case the *radiological* impression was that of a *cecal mass* (was read by four radiologists). Therefore, gastroenterologists should entertain the diagnosis of cecal gangrene in a patient with acute right lower quadrant pain.[figure1]



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#### Case Series on Hepatic Portal Venous Gas

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**Purpose:** Hepatic portal venous gas (HPVG) is an important, but rare radiographic finding of gas in the portal venous system. It is a valuable clue to a serious intraabdominal pathology. We present 2 contrasting cases of bowel ischemia causing HPVG.

**Methods:** Review of literature using Medline.

**Results:** A 62 year old male presented with diffuse abdominal pain, associated with abdominal distension, constipation, nausea & vomiting for 3 days. He was found to be in septic shock. CT of the abdomen and pelvis showed air in the portal venous system, distended loops of small bowel with air fluid levels, along with air in the mesenteric veins. At surgery, perforated appendix & cecum with purulent peritonitis was found & compromised bowel was resected. Histopathology revealed acute appendicitis; the small bowel segment showed extensive hemorrhage, with ischemic necrosis of the muscularis propria. Vascular structures were free of thrombi or emboli. A 68 year old female presented with dizziness & lightheadedness for a day. She reported feeling of mild abdominal discomfort in the left lower quadrant. Initial blood pressure was 78/34. CT scan of the abdomen & pelvis revealed gas in the left hepatic lobe in a branching pattern within the intrahepatic portal venous radicals. Repeat CT scan 3 days later, revealed bowel wall thickening at the cecum with pericolic inflammatory changes. Because of worsening leucocytosis and acidosis, surgery was done. This revealed a cecal inflammatory mass without perforation. Histopathology revealed ischemic changes of the cecum. Cecum is considered a watershed zone vulnerable to ischemia. HPVG was caused by localized cecal ischemia due to severe hypotension caused by her antihypertensive medications. The first case presented

with dramatic clinical features versus the second case, which showed minimal clinical signs and symptoms. Ischemia caused by hypotension was the initiating event in both patients, with sepsis & overtreatment of hypertension being the primary causes in respective cases.

**Conclusion:** HPVG is a serious diagnostic clue indicating bowel compromise. The cause of HPVG should be thought of as a surgical emergency until proven otherwise, as a delay in surgical intervention can be fatal.

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#### Isolated Polypoid Ganglioneuroma of the Sigmoid Colon

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**Purpose:** Ganglioneuromas (GN) are rare tumors and seldom arise in the gastrointestinal tract. GN are often located in the posterior mediastinum, retroperitoneum, adrenal glands, pelvis, cervix & parapharyngeal region. We report a case of isolated polypoid GN in a 56-year-old caucasian male who underwent a screening colonoscopy.

**Methods:** Review of available literature using Medline.

**Results:** Patient's past medical history & physical examination was unremarkable. Family history was noncontributory. All hematological & biochemical investigations were normal. Colonoscopy revealed a sessile 15 mm submucosal polyp located about 20 cm proximal to the rectosigmoid junction. Macroscopically, the specimen was a 20 × 20 × 20 mm pale brown polyp. Microscopic examination demonstrated the presence of ganglion cells and spindle cells. Immunoperoxidase staining with S-100 protein showed positive areas in the spindle cell regions, ganglion cells & prominent nerve fibers. The pathological diagnosis was made as polypoid GN. A surveillance colonoscopy after 2 months showed no other abnormalities. Polypoid GN differ from diffuse intestinal GN in that the neural proliferation lies within the lamina propria, thus giving the clinical impression of a 'micropolyp'. Differential diagnoses include neurofibroma & schwannoma, which are notable for the absence of ganglion cells. Isolated GN does not produce any specific symptoms & are usually noted incidentally at colonoscopy, surgery or necropsy. There have been some reports of abdominal pain, obstruction, constipation, ileus, appendicitis & weight loss as presenting clinical scenarios based on the size and the position of the tumor. The lesions can be dumb-bell shaped & luminal resection can increase the risk of perforation. Patients with isolated polypoid GN do not require long-term follow-up since they do not develop systemic disease. Diffuse GN is however associated with Von Recklinghausen's disease, Cowden's disease, Multiple Endocrine Neoplasia (MEN) type 2B & non familial adenomatous polyposis. They have been shown to be caused by a single mutation in the RET proto-oncogene, with a methionine to threonine substitution at codon 918 (M918T).

**Conclusion:** Because of the potential risk of perforation of the colon by GN, gastroenterologists must therefore be aware of this rare but important identity.

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#### Complicated Periappendiceal Abscess Diagnosed on Colonoscopy

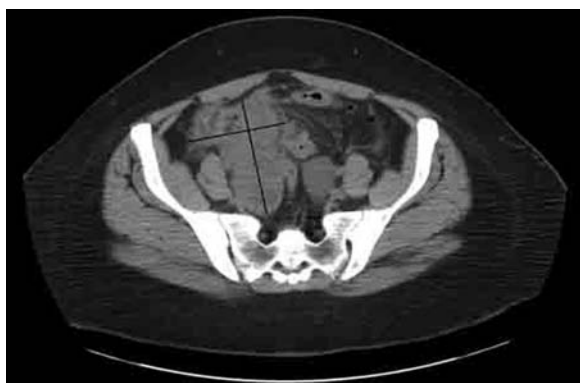
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**Purpose:** Appendicitis with its complications like periappendiceal abscess is diagnosed with 93% to 98% accuracy using CT. In several reported cases, appendicitis with atypical symptoms and/or nondiagnostic imaging was diagnosed during colonoscopy. We present a case of complicated periappendiceal abscess diagnosed on colonoscopy.

**Case Report:** A 37 yr old female presented to our clinic being referred for an abnormal CT scan showing mass extending into the cecum. She had intermittent right lower quadrant pain for past 2-3 months, increasing in

intensity with menstruation. She had no change in bowel movements, no urinary symptoms, no nausea or vomiting. CT abdomen showed right pelvic cystic mass attached to the uterus, adnexa, cecum and sigmoid colon with no visualization of appendix (Fig. 1). Colonoscopy showed edematous cecum with clear pus extruding from the appendiceal orifice confirming appendicitis (Fig. 2). Laparotomy showed large mass in the pelvis covered with omentum and small bowel. Pus was expressing from necrotic base of the appendix and from the right ovarian cyst. Appendectomy and hysterectomy with bilateral salpingo-oophorectomy were performed. Pathology confirmed appendicitis with abscess formation along with the ovarian abscesses on both sides. The culture from the pus was positive for *Bacteroides fragilis* indicating bowel as the source of infection. Our patient had appendicitis with abscess that disseminated causing infection of the ovarian cysts. The infection was walled off by omentum causing atypical symptoms, thus misleading physicians till colonoscopy.

**Conclusion:** This unusual case illustrates a key role played by colonoscopy in diagnosing a complicated periappendiceal abscess presenting with atypical symptoms and non diagnostic radiologic workup.[figure1][figure2]



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#### Cisplatin Induced Ischemic Colitis: A Case Report

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**Purpose:** Ischemic colitis (IC) is caused by a reduction in intestinal blood flow, which most commonly arises from occlusion, vasospasm, and/or hypoperfusion of the mesenteric vasculature. The development of IC in setting of chemotherapy is rare. We report a case of a 68-year-old woman who developed IC involving the descending colon after chemotherapy with Cisplatin.

**Case:** A 68-year-old woman who was on Cisplatin for invasive thymoma presented with 4-day history of nausea, vomiting, left sided crampy abdominal pain and bloody diarrhea. The symptoms started 2 days after the first cycle of chemotherapy. Her past medical history included asthma, bronchiectasis, colonic diverticulosis, peptic ulcer disease and migraines. The patient was taking premarin, omeprazole, and denied any NSAID use. The patient also denied personal or family history of inflammatory bowel disease. The patient had stable vital signs, and the physical examination demonstrated mild left lower quadrant abdominal tenderness. Laboratory studies revealed mild leukocytosis. A CT scan of the abdomen revealed diffuse thickening of the colon wall with edema and fat stranding in pericolic region from the level of the splenic flexure through the upper sigmoid colon, and the abdominal vasculature was patent. A colonoscopy revealed areas of diffuse mucosal edema and erythema with superficial exudates from 30 cm to 80 cm from anal verge. The stool studies and colonic biopsies were negative for an infectious etiology, and the biopsies were consistent with IC. The patient was thought to develop IC secondary to Cisplatin chemotherapy.

**Discussion:** IC after systemic chemotherapy has been described, but is exceedingly rare after Cisplatin. There is only one published case report in English literature of IC related to cisplatin by Maurya et al. Their patient received Docetaxel with Cisplatin. Although rare, IC should be considered in patient with colitis symptoms after Cisplatin chemotherapy.

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#### A Rare Mimic of Colon Cancer: Ameboma

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**Purpose:** To appreciate the diagnostic challenge posed by ameboma in a patient encumbered with multiple ailments as well as to gain a brief insight into its clinico-pathological features and treatment options.

**Results:** A 76-year-old male from Minnesota, with history of non-small cell lung cancer and prostate cancer, presented with subacute intestinal obstruction and hematochezia. He had recently started prednisone for radiation pneumonitis. Computed tomography of the abdomen revealed circumferential colonic wall thickening and exophytic masses extending from the cecum to the proximal transverse colon. Colonoscopy revealed multiple, partially obstructing, necrotic luminal masses in the same distribution. The differential diagnoses included extensive colon cancer, metastatic cancer, lymphoma, tuberculosis, and *Yersinia* colitis. A biopsy done to ascertain colon cancer showed instead hemophagocytic *Entamoeba histolytica* in flask-shaped ulcers confirming the diagnosis of ameboma. High serum anti-*E. histolytica* antibody titers and trophozoites and cysts in the stool provided corroborative evidence. The clinical enigma was resolved when subsequent questioning revealed that he was a frequent traveler to Central America and China, the last visit being 5 years ago. Treatment with Metronidazole for 3 weeks followed by Paromomycin for a week culminated in clinical and colonoscopic resolution.

**Conclusion:** *E. histolytica*, a leading cause of parasitic death in developing nations, represents a significant health hazard for international travelers. Intestinal amebiasis is typified by colonic ulcero-inflammatory lesions and manifests as a clinical spectrum ranging from asymptomatic infection, through colitis, ameboma and toxic megacolon. Ameboma, a rare presentation even in endemic countries, is characterized by an inflammatory colonic mass indistinguishable from colon cancer. Complications include bleeding, bowel obstruction and perforation. As exemplified here, immunosuppression may precipitate severe symptoms in asymptomatic carriers several years after the sentinel infection. Metronidazole is the cornerstone of therapy followed

by a luminal amebicide such as Paromomycin or Diloxanide furoate to eradicate colonization. Colonic mass in the setting of immunosuppression and a history of travel to developing countries, even in the remote past, should raise the possibility of ameboma. Prompt diagnosis and treatment is imperative to prevent complications and unnecessary surgery.

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### Two Primary Adenocarcinomas in a Crohn's Patient with Infliximab Therapy

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**Purpose:** A 55 year old woman with a six year history of Crohn's disease presented with recurrent episodes of pancreatitis. The patient was initially diagnosed with Crohn's disease of the stomach and duodenum, without involvement of the colon and remainder of the small bowel. One year following diagnosis, the patient had continued progressive obstructive symptoms and a loop gastro-jejunostomy was performed for a duodenal stricture. Following surgery, she received therapy with azathioprine and eventually infliximab. After approximately three years of therapy with infliximab, the patient developed severe abdominal pain and was diagnosed with pancreatitis. Azathioprine was discontinued; however, she experienced a recurrent episode of pancreatitis the following month. A CT scan revealed mild dilatation of the pancreatic duct without a discrete mass, intra/extrahepatic biliary dilatation, and wall thickening with enhancement in the second portion of the duodenum. An MRCP confirmed wall thickening just proximal to the ampulla, without a ductal filling defect. An endoscopy was performed to locate the ampulla and characterize Crohn's disease involvement. While the stomach appeared grossly normal, a stricture of the duodenum was appreciated 5 cm past the pylorus and biopsied. The efferent limb of jejunum appeared normal, but the afferent limb contained an area of stricturing disease and the ampulla could not be located with a side-viewing endoscope. Biopsies of the duodenal stricture revealed adenocarcinoma. A pancreaticoduodenectomy was performed with resection of a portion of the gastric antrum. A Stage I (pT1, N0) well to poorly differentiated adenocarcinoma of the periampullary duodenum was found in a background of segmental Crohn's duodenitis with inflammatory stenosis and polypoid/flat high grade dysplasia. In addition, a signet ring cell adenocarcinoma of the pyloric channel was found, Stage IB (pT2a, N0), in a background of chronic gastritis with high grade dysplasia. There was no tumor invasion of the pancreatic/biliary ducts and 33 regional lymph nodes were negative for adenocarcinoma. This case of two adenocarcinomas in a young patient with a short duration of Crohn's disease raises concern about the relationship between infliximab and tumorigenesis.

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### Primary Sclerosing Cholangitis and Autoimmune Hemolytic Anemia: A Casual Association?

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**Purpose:** Primary sclerosing cholangitis (PSC) is a progressive and incurable condition characterized by inflammation, fibrosis, destruction and loss of interlobular-sized bile ducts, leading to biliary cirrhosis and liver failure. It is more common among men, is frequently associated with chronic inflammatory bowel disease (IBD) and with the following HLA haplotypes, -A1, -B8, and -DR3. Patients with PSC have increased prevalence of other autoimmune disorders, e.g. celiac disease. Autoimmune hemolytic anemia (AIHA) has been described in association with PSC, albeit uncommonly.

A 55 year-old man with stable PSC, confirmed the previous year, and treated hypothyroidism but without chronic IBD, complained of increasing fatigue, chest pain and dyspnea of two weeks' duration. He denied overt blood loss, fever, pruritus or jaundice. The principal examination findings were pallor and icterus. Vital signs were stable. Heart sounds were normal, there was no pericardial friction rub and both lung bases were clear. Neither liver nor spleen was palpable, and he had no clinical evidence of ascites. Laboratory data were as follows: Hb 6.7 g% (normal range [NR]: 14–18), and MCV 108.6 fL (NR: 80–94), with normal white cell and platelet counts. The reticulocyte count was 6.2% (NR: 0.5–4). LDH concentration was 164 IU/L (NR: 91–180). However, the serum haptoglobin was 2 mg% (NR: 36–195). His polyspecific, direct antiglobulin test was positive. Serum concentrations of ferritin, folate and vitamin B12 were normal. Total serum bilirubin (BR) was 3.5 mg% (NR: 0.4–1.2), of which the indirect component was 2.6 mg%. The alkaline phosphatase was 420 IU/L (NR: 42–121), but aminotransferase concentrations were normal. Albumin was 4 g% (NR: 3.2–5.5), and his prothrombin time was 12 seconds (NR: 9–13.1). Although his EKG revealed new left bundle branch block, cardiac enzymes were not elevated. A presumptive diagnosis of AIHA was made and treatment with methyl prednisolone begun. Concentrated red cells were transfused cautiously. Four weeks after commencing corticosteroid therapy his Hb had risen to 13.2 g%, and the haptoglobin to 37.8 mg%. His BR was 1.3 mg%. The daily dose of prednisone was 40 mg.

Reports of the co-existence of PSC and AIHA include the sequence described above, and *vice versa*. This is the first report to our knowledge of a patient with PSC, AIHA and autoimmune hypothyroidism. The corticosteroid exposure demands careful attention to minimization of bone density loss.

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### Henoch-Schönlein Purpura with Terminal Ileitis Masquerading as Crohn's Disease

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**Purpose:** An 18 year-old Korean male presented with a 1-week history of colicky abdominal pain, non-bloody diarrhea and painful swelling of his right ankle. His PMH, FHx and SHx were unremarkable. Upon initial evaluation, he was febrile, tachycardic and tender with palpation of his RLQ. His right ankle appeared warm and swollen without any evidence of rash. Admission labs: WBC:18, H/H: 18/48, Plt: 400, BUN:11, Cr: 1.0. AXR was normal. ABD CT scan revealed a mildly dilated and thickened terminal ileum with a normal appendix. Initial differential diagnosis included: Crohn's disease with extra-intestinal manifestations, infectious colitis and diverticulitis. Additional labs: ESR: 6, CRP: 4.4. Colonoscopy showed a normal rectum and colon and terminal ileitis with localized edema, erythema and purulent, superficial ulcerations. Given these findings, a presumptive diagnosis of Crohn's disease was made and the patient was started on a 5-ASA regimen. Biopsies from the terminal ileum revealed chronic active ileitis with ulceration and fibropurulent exudate. Additional labs: ASCA(+), p-ANCA (–), negative blood, urine and stool cultures. Seven days after discharge, the patient represented appearing toxic with RLQ pain and a new bilateral lower extremity purpura with associated polyarthritides. Labs revealed: WBC:14, H/H: 14/42, Plt:450, Eos:2, ESR:53, CRP:6.7, BUN:77, Cr:2.5 with nephrotic range proteinuria and a normal coagulation profile, peripheral smear, hepatitis panel and rheumatologic serologic evaluation. An IgA level was mildly elevated at 464. Kidney biopsy showed large irregular mesangial subepithelial deposits and a skin biopsy demonstrated small vessel leukocytoclastic vasculitis. Given the constellation of these new findings including palpable purpura in the absence of coagulopathy, abdominal pain, arthritis and a biopsy with predominant IgA deposition, a diagnosis of Henoch-Schönlein purpura (HSP) with terminal ileitis was made. The patient was started on prednisone with a rapid clinical improvement and normalization of renal function.

HSP is a small-vessel vasculitis that commonly affects the skin, joints, kidneys and gastrointestinal tract. GI manifestations typically occur up to 8 days after the onset of purpura. However, as in this case, the diagnosis of HSP may be delayed not only when the GI manifestations mimic other entities such as Crohn's disease, but also, when the GI manifestations precede the characteristic purpuric rash.

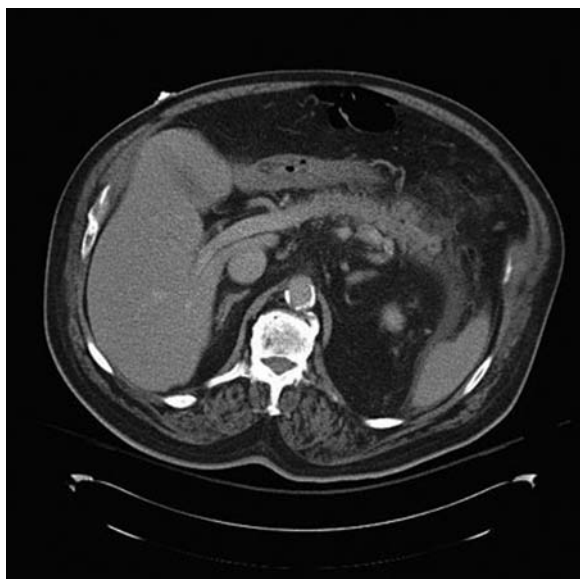
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### Acute Pancreatitis: An Unusual Complication of Double Balloon Enteroscopy

Rahul Pannala, MD, Ganapathy A. Prasad, MD\*, Suresh T. Chari, MD, Louis M. Wong Kee Song, MD. Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN.

**Purpose:** 76 year old male with critical aortic stenosis presented for evaluation of transfusion-requiring iron deficiency anemia. As esophagoduodenoscopy, colonoscopy, capsule endoscopy, and CT enterography were unremarkable, a double-balloon enteroscopy (DBE) was performed and revealed a moderate sized jejunal vascular ectasia that was treated with argon plasma coagulation. There were no immediate procedure-related complications.

Approximately 4 hours later he presented with severe abdominal pain. Significant laboratories included a markedly elevated lipase (924 U/L [10–73 U/L]) and amylase (380 U/L [26–102 U/L]). CT abdomen revealed inflammatory changes in the body and tail of the pancreas and significant edema in the peripancreatic fat (Fig. 1) but there was no evidence of necrosis. He improved gradually over the course of the next week with conservative treatment. CT abdomen 2 months (Fig. 2) later demonstrated persistent inflammatory changes in the pancreatic body and tail and ill-defined fluid collections in and around the pancreatic tail. However, the patient was asymptomatic. Repeat CT 6 weeks later noted decrease in size of the fluid collections and pancreatic inflammation. He had an uneventful aortic valve replacement at this point. CT performed 4 months later demonstrated a normally enhancing pancreas with minimal residual fluid collection. Our report adds to previous case reports from Japan and Netherlands of this uncommon complication of DBE. Though there are no prospective series, the estimated prevalence of pancreatitis following DBE is around 1%. The etiology of pancreatitis following DBE is unclear but may be related to duodenal reflux or transient sphincter of Oddi dysfunction, which may occur during a long procedure such as DBE with compression of the ampulla. Prospective evaluation of the complications of DBE is needed.[figure1][figure2]



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### Insulin Therapy for Hypertriglyceridemia (>6,000 mg/dl) and Hyperglycemia (>500 mg/dl) in the Setting of Acute Pancreatitis

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**Purpose:** Hypertriglyceridemia (HTG) accounts for 2% of acute pancreatitis. The most common presentation of HTG pancreatitis is uncontrolled diabetes. Control of triglyceride levels is essential to avoid exacerbation of pancreatitis. Insulin therapy for HTG in the setting of pancreatitis is not widely reported.

**Results:** A 25 year-old female with Type II diabetes and hypertension with poor medication compliance presented to the emergency room complaining of abdominal pain and several episodes of non-bloody, non-bilious emesis. She denied fevers or chills. She also denied alcohol or drug use. Family history was unremarkable. Exam revealed a distended, tender abdomen without guarding or rebound and decreased bowel sounds.

Blood sample was grossly lipemic and showed: HTG (6,280 mg/dl), elevated lipase (7,430 u/l), and hyperglycemia (566 mg/dl). Pregnancy and toxicology tests were negative. Abdominal CT confirmed pancreatitis without evidence of gallstones or biliary ductal dilatation/obstruction.

An insulin (0.1 u/kg/hr) intravenous (IV) drip was started and enteral nutrition withheld. Twenty hours later, triglyceride levels decreased to 1,658 mg/dl and to <500 mg/dl by hospital day 5. Serum glucose levels decreased to 82 mg/dl after 24 hours. Serum lipase levels decreased to <60 u/l in one week.

**Conclusion:** Reported treatments of HTG pancreatitis include combinations of IV insulin, IV heparin or apheresis. We managed HTG with IV insulin, which activates lipoprotein lipase and degrades triglycerides into glycerol and fatty free acids. In addition, IV insulin also treated hyperglycemia. Heparin has been used with insulin for HTG for its ability to release lipoprotein lipase from endothelial surfaces. However, lipase released by heparin is more liable to hepatic degradation, depleting plasma stores. Apheresis can rapidly remove triglycerides. However, the efficacy of apheresis in HTG pancreatitis has limited data and conflicting reports. We felt apheresis was unnecessary in our patient due to the decrease in triglyceride levels after 24 hours of IV insulin.

IV insulin can successfully manage HTG and hyperglycemia in the setting of acute pancreatitis and uncontrolled diabetes. However, definitive recommendations for therapy in HTG pancreatitis requires further study.

Reported cases of *C. difficile* bacteremia and sepsis

Author	Age (yr)/ Sex	Clinical presentation	Other isolated organisms	Stool toxin	Suspected source	Treatment	Outcome
Feldman et al.	85 F	Fever, hypotension, diarrhea	<i>Enterococcus faecalis</i>	Pos	Colon	Vancomycin/ Gentamicin iv	Ventilator dependent
Wolf et al.	18 M	SBO	<i>Candida parapsilosis</i>	NR	Unknown	NR	Favorable
Wolf et al.	33 F	Pelvic abscesses, rectovaginal fistula	<i>C. cadaveris</i> , <i>B. melaninogenicus</i> , <i>Fusobacterium species</i>	NR	Pelvic abscesses	NR	Death
Wolf et al.	77 M	Sigmoid perforation	<i>Eubacterium lentum</i>	NR	Colon	NR	Death
Cid et al.	3 M	Tonsillitis, pericarditis	None	NR	Unknown	Vancomycin iv	Favorable
Byl et al.	18 M	Fevers, abdominal pain, diarrhea	None	Pos	Colon	Vancomycin oral	Favorable
Byl et al.	78 M	Pneumonia, diarrhea	None	Neg	Colon	Vancomycin oral and iv	Death
Spencer et al.	65 M	Gangrenous toe, diarrhea	<i>Bacteroides fragilis</i>	Neg	Unknown	Cefuroxime/ Metronidazole iv	Death
Sanchez et al.	51 F	Hepatic abscess, biliary obstruction	<i>Enterococcus casseliflavus</i>	NR	Unknown	Daptomycin/ Metronidazole iv	Favorable

SBO = Small bowel obstruction, Pos = Positive, Neg = Negative, NR = Not reported

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### ***Clostridium difficile* Sepsis Associated with an Enterococcal Hepatic Abscess**

Patricia A. Sanchez, MD, Michael Selden, MD, Owen J. Smith, MD, Wendell K. Clarkston, MD\*. Department of Medicine, Division of Gastroenterology, University of Missouri at Kansas City School of Medicine, Kansas City, MO.

**Purpose:** A 51-year-old female with metastatic gallbladder carcinoma and recurrent biliary obstruction presented with fevers, hypotension, right upper quadrant tenderness and jaundice. She denied diarrhea and other gastrointestinal complaints. Blood cultures identified Vancomycin-resistant *Enterococcus casseliflavus* and *Clostridium difficile*.

Laboratory data included a WBC of 22,000/ $\mu$ L an ALT of 168 IU/L, alkaline phosphatase of 513 IU/L and a total bilirubin of 8 mg/dL.

Imaging revealed a 9-cm hepatic abscess and dilated bile ducts both of which were percutaneously drained by interventional radiology. Cultures of the biliary aspirate grew *Enterococcus faecium* but no anaerobes. The patient responded to intravenous daptomycin and metronidazole.

**Discussion:** *C. difficile* is a major nosocomial enteric pathogen that results in significant morbidity. While its primary presentation is that of acute colitis, extraintestinal manifestations have been described (Table 1). Whether the source of the bacteremia in our case was colonic or biliary is difficult to determine.

Physicians should be cognizant of the potentially invasive nature of this organism. Extraintestinal manifestations may become more frequent given the increased incidence and virulence recently associated with this microorganism.

## 634

### **Delayed Post-Polypectomy Bleeding Associated with Use of Bilberry (*Vaccinium Myrtillus*) Extract**

Mitchell Duterte, MD\*, Shawn Waugh, PA-C, Rizwana Thanawala, MD. Lake City, FL.

**Purpose:** The use of herbal medications is becoming more common. Since these are considered dietary supplements, they are not subject to stringent regulations by the Food and Drug Administration. Published data on the adverse effects of herbal medications are scanty and this may have significant implications on the perioperative care of patients.

A 66 year old man with history of diabetes mellitus and hypertension underwent colonoscopy for colorectal cancer screening. He takes several medica-

tions, none of which are anticoagulants, antiplatelets or anti-inflammatory drugs. The patient also takes bilberry extract 500 mg once a day, supposedly to improve his vision. Since the adverse effects of bilberry extracts are not known, the patient was told to stop taking it one week before the procedure. Colonoscopy showed multiple colon polyps, the biggest of which was a 1 cm sessile polyp in the transverse colon. These were removed by snare cautery using standard technique. The immediate post-colonoscopy course was uneventful. Two weeks after colonoscopy, the patient resumed taking bilberry extracts. Two days later, he started to have hematochezia. His hemoglobin dropped from 13 g/dl to 6.8 g/dl. The platelet count was 139 thou/cu mm. Bleeding time was prolonged at >15 minutes. The patient was transfused a total of 11 units pRBC. Repeat colonoscopy revealed that the bleeding was from the polypectomy site at the transverse colon, where an ulcer with active oozing of blood was seen. The bleeding site was cauterized with gold probe and clipped with three hemoclips. The bleeding ceased for 24 hours. However the patient started to bleed again. Because of failure of endoscopic hemostasis, he subsequently underwent subtotal colectomy. The post-operative course and the remainder of the patient's stay in the hospital was unremarkable.

Extracts of bilberry (*V. myrtillus*) have been used for many years in the treatment of diarrhea, dysmenorrhea and a variety of visual disorders. It has several bioactive components but most of the studies have been on anthocyanosides. Anthocyanins are purported to have antioxidant, hypoglycemic and lipid-lowering properties. It has also been shown to inhibit platelet aggregation and inhibit the synthesis and release of pro-inflammatory agents like prostaglandins, leukotrienes and histamine. Theoretically it may increase the risk of bleeding. However human studies proving its efficacy and safety are lacking. Therefore it may be prudent to stop this medication in patients undergoing procedures where the risk of bleeding is high.

## 635

### **Mycophenolate Mofetil (MMF) Induced Cecal Ulceration in a Patient with Lupus Nephritis**

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**Purpose:** Lupus nephritis (LN) remains a major cause of renal failure in women of child bearing age. In comparison to cyclophosphamide, MMF has an excellent safety profile. MMF is usually associated with gastrointestinal (GI) side effect, especially diarrhea is a major concern. More serious events such as GI bleeding or colon perforation were reported in transplantation

group. We describe a case of cecal ulceration and GI bleed with the use of relatively high dose of MMF in a patient with LN.

A 38 year old African American woman with systemic lupus for 8 years developed active LN class IV/V. She was initially placed on oral cyclophosphamide 2 mg/kg and methylprednisolone 16 mg daily. Cyclophosphamide was switched to MMF 2 grams/day because of leucopenia. The dose of MMF was increased to 2.5 gm/d for the persistent nephrotic syndrome, with improvement of the proteinuria. However she developed diarrhea and severe anemia requiring blood transfusion. Colonoscopy revealed erythematous mucosa from hepatic flexure to cecum with two oozing linear ulceration in cecum. With a temporal association between the dose increment of MMF and the event, MMF was discontinued. Her GI bleeding resolved in 3 days. Colonoscopy was repeated in 4 weeks revealing complete resolution of the ulcers. Severe GI adverse effects like upper GI bleeding and ulcerations are reported with the use of MMF but there are very few reports of cecal ulceration in the literature.

The frequency of adverse effects seems to be related to higher blood level of MMF, whereas immunosuppressive activity is related to the total exposure (Area under the curve). High dose of MMF inhibits the proliferation of basal epithelial cells of intestine in mice.

Owing to its safety and efficacy as shown in recent trials, MMF is gaining popularity as a therapeutic option both for induction and maintenance of severe LN. Even with use of higher doses of MMF, monitoring of drug level is not routinely used. In view of increasing use of MMF the likelihood of encountering these serious side effects are higher. Future studies are needed to determine both effective and safe therapeutic targets to make this promising agent more safe and predictable.

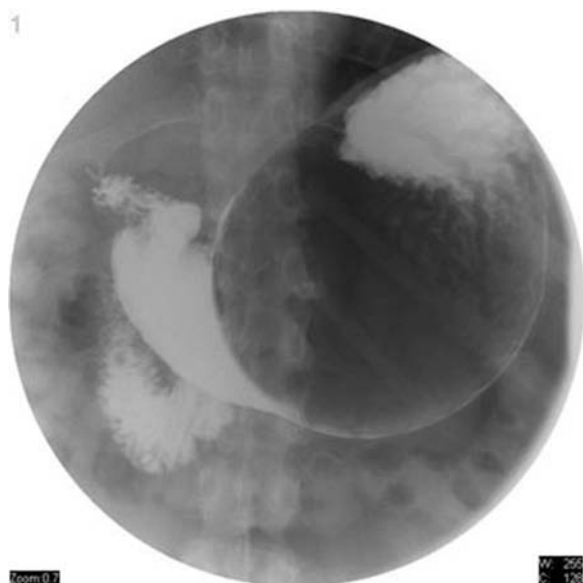
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#### Intragastric Balloon for Obesity Causing Gastric Outlet Obstruction

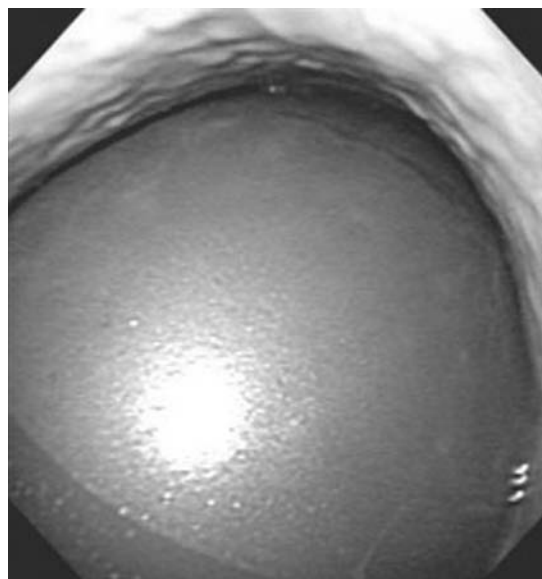
Natalee S. Sansone, MD, Liberato Salvatore, MD\*. Internal Medicine, Division of Gastroenterology, New York Hospital of Queens, Flushing, NY.

**Purpose:** Intragastric balloons are indicated for treatment of moderately obese patients. Major complications include immediate gastric outlet obstruction, spontaneous deflation causing obstruction, and gastric perforation. We report a case of delayed gastric outlet obstruction.

A 59 yo female presented with nausea, vomiting and abdominal pain for 5 days. The patient had an intragastric balloon (BioEnterics Intragastric Balloon – BIB, INAMED Health, Santa Barbara, CA) placed 9 weeks prior in Mexico having lost 30 lbs with a BMI of 35 kg/m<sup>2</sup>. Past history included GERD and laparoscopic cholecystectomy.



Her vital signs were stable. Her RUQ and epigastrium were firm and tender. Serologies showed: Na 137, K 2.6, Cl of 91, CO<sub>2</sub> 35, glucose 127, BUN 18, and creatinine 1.4. Upper GI series showed positional barium passage (Fig. 1). [figure1] Endoscopy, using Olympus GIF 140 (Olympus Corp), showed a fundal balloon occluding the lumen (Fig. 2). A scleroneedle and a rat tooth forcep were used to puncture the balloon and drain its contents. The endoscope was reinserted with an overtube (Bard Endoscopic Overtube). A jumbo snare was used to impact the balloon into the overtube at 10 cm. All were removed in unison with anesthesia on standby. [figure2] The following day, the patient complained of a sore throat and chest pain and had a temperature of 38.8. The leukocyte count was 11.93 K/uL (normal 4.8–10.8 K/uL). CT scan of the neck and chest showed a small amount of air in the paraesophageal space and mediastinum.



The patient was treated with piperacillin/tazobactam 4.5 grams q8<sup>h</sup> IV, metronidazole 500 mg q6<sup>h</sup> IV, gentamicin 240 mg IV daily and made NPO. She was discharged 10 days later.

In conclusion, a delayed gastric outlet obstruction occurred after intra-gastric balloon placement. Endoscopic balloon removal with overtube assistance was complicated by a small esophageal perforation, managed conservatively.

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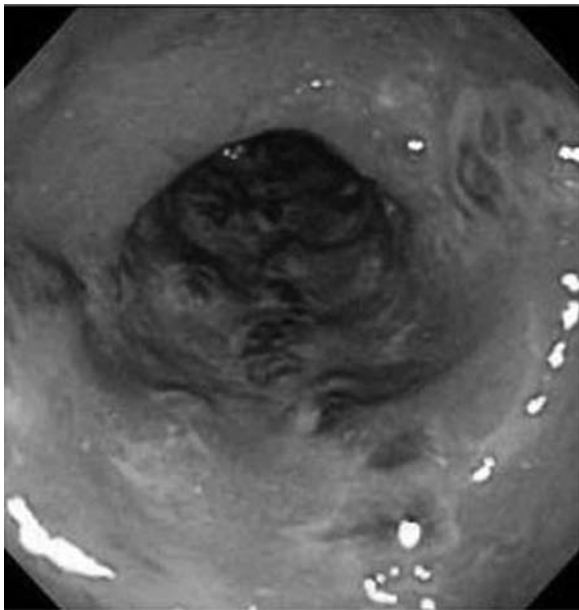
#### Heat Stress and Exercise Induced Ischemic Colitis in a 21 Year Old

Riffat Meraz, MD, Namita Chittoria, MD, Preeti Mehta, MD, Uma Murthy, MD\*. Internal Medicine, SUNY Upstate Medical University, Syracuse, NY.

**Purpose:** A 21 year old healthy caucasian male presented with vomiting, diarrhoea and LLQ abdominal pain within 2 hours of vigorous game of frisbee on a hot day of July with T Max of 88° F. Stools were loose, brown with bright red bloody streaks and vomitus was large volume containing food. He denied ingesting restaurant or undercooked food, use of antibiotics or NSAIDs, recent travel, ano rectal intercourse, h/o joint pain, skin rash, eye symptoms or any such previous episode.

Exam was significant for dry oral mucosa with poor skin turgor and LLQ tenderness with DRE positive for occult blood. Labs were significant for CPK of 719, Alk Phosphatase 174, WBC 22.6. Stool studies, vasculitis panel and coags were negative. His CT abdomen showed increased soft tissue stranding and thickening of transverse and descending colon suggestive of inflammation or infection. Colonoscopy showed severe segmental inflammation characterized by congestion, erythema, friability with granularity at the transverse colon and splenic flexure, with multiple linear bluish lesions suggestive of Ischemic Colitis. Biopsy was done and results were consistent

with *Ischemic Colitis*. [figure1]Patients clinical condition and biochemical parameters improved with IVFs and bowel rest within two days, and he was discharged home in a stable condition.



Heat stress causes acute-phase, thermoregulatory response with cutaneous vasodilation and splanchnic vasoconstriction. One of the most serious complications include *Intestinal ischemic or infarction*, usually in children and elderly.<sup>1</sup> And elevated body temperature alone may not be the sole cause of fatal outcomes in heat stroke but that toxic chemicals released in this accelerated thermogenesis may also be involved.<sup>2</sup>

The threat of heat-related illnesses is increasing with global warming and although they are treatable and preventable, at least 688 persons die of them in the US each year.<sup>3</sup> *Ischemic colitis must be suspected in heat stressed patients even if they are young and even if their core temperature is <40° C at presentation.*

1. NEJM, Vol. 346, No. 25 – June 20, 2002
2. J Sci Med Sport. 2007 May 22
3. Heat-related deaths–US, 1999–2006. MMWR 2006; 55(29):796–8.

## 638

### Intra Abdominal Pathology in Polymyalgia Rheumatica Presenting as Exacerbation of Rheumatic Disease

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**Purpose:** A 73 year old lady with polymyalgia rheumatica presented with a month's history of right hip and thigh pain and stiffness. She had had intermittent diarrhoea with no bleeding or mucus.

Examination revealed reduced right hip and knee flexion only. She was afebrile with elevated white cell count and inflammatory markers.

Hip, pelvic xrays, stool culture were normal. Sigmoidoscopy revealed mild proctitis and mild diverticulosis. Ultrasound scan abdomen was also normal. She had been commenced on steroids 3 weeks prior to admission.

A diagnosis of polymyalgia exacerbation was made and steroid dose increased. Antibiotics were also commenced.

Diarrhoea was not recorded during admission but limb weakness and hip pain deteriorated and inflammatory markers continued to rise, so an MRI spine and pelvis was arranged on day 5.

This revealed multiple gluteal abscesses extending around the right femoral head along with a perforated diverticulum and presacral abscess.

Despite attempted radiologically guided drainage with a view to hemicolectomy if required, and escalating antibiotic therapy, she became increasingly septic and died.

**Case 2:** A 69 year old lady with polymyalgia presented with a 3 week history of left thigh pain. She had had left sided abdominal pains for 6 months treated by oral analgesia. Bowels chronically alternated between constipation and diarrhoea with no rectal bleeding. She had loss of appetite and weight over three months. Examination revealed mild weakness of left hip flexion. White cell count and CRP were elevated. A diagnosis of exacerbation of polymyalgia was made and steroid dose increased.

She was admitted a week later with severe abdominal pain, tachycardia and pyrexia. Examination revealed generalized peritonitis. After aggressive resuscitation, laparotomy was performed. This revealed faecal peritonitis due to obstructing proximal sigmoid tumour with a perforated descending colon and a large retroperitoneal abscess. She had a prolonged stay in the intensive care unit following Hartmann's procedure, but was later found to have liver metastases.

**Discussion:** These cases highlight how patients with polymyalgia may have perforated intrabdominal disease which mimics their rheumatic pathology. Steroid therapy which is the mainstay of polymyalgia therapy can be detrimental.

In the presence of diarrhea/abdominal pain, a high degree of clinical suspicion should be maintained for an alternative gastrointestinal cause.

## 639

### Enteryx Revisited

Matthew Weed, MD\*, Steven A. Gorcey, MD, Shannon Hammond, FNP. Gastroenterology, Monmouth Medical Center, Long Branch, NJ and Brody School of Medicine, Greenville, NC.

**Purpose:** Enteryx was voluntarily recalled due to adverse events including one death due to an aorto-enteric fistula. During training, endoscopists are instructed to inject the polymer at the Z-line.

**Methods:** Our technique, namely injecting at or below the diaphragmatic hiatus, rather than at the EG-junction, significantly reduces the risk of complications. We present three patients that, when used appropriately, could benefit from Enteryx.

**Results:** LM presents with retrosternal burning, dysphagia, recurrent URI. She had been treated with PPIs and cycles of antibiotics. pH study demonstrated significant reflux. EGD revealed esophagitis and a 2 cm sliding hiatal hernia. She was referred for a fundoplication but opted for the Enteryx. Two weeks later she had a decrease in her GERD and URI symptoms. AH has severe reflux, severe asthma and retrosternal chest pain. Cardiac work up was negative. EGD showed erosive esophagitis. Manometry showed ineffective peristalsis. pH study demonstrated significant acid reflux. High dose PPI and promotility agents provided no relief. She was referred for laparoscopic fundoplication. She could not be cleared for general anesthesia. Enteryx was performed. Three weeks later there was marked improvement in her chest pain and asthma symptoms. She decreased Nexium from 80 mg twice daily to 40 mg once daily. Within 9 months she had recurrence of her symptoms. Work-up revealed loss of polymer. Repeat Enteryx would have been considered but unavailable due to the recall. MD presents with a history of chronic GERD and two Nissen fundoplications. The first fundoplication had "slipped." He reported recurrent regurgitation and substernal discomfort despite high dose PPI and promotility agents. Endoscopy was unrevealing. Manometry showed normal motility with presence of a high-pressure zone consistent with fundoplication. The Enteryx procedure was offered to the patient. The polymer was injected just distal to the diaphragmatic hiatus. The patient had almost immediate response. Over several months he had recurrence of symptoms. EGD and X-ray revealed loss of polymer. The Enteryx procedure was performed using the same technique. The patient again reported immediate relief of symptoms.



**Conclusion:** Enteryx complications could be avoided by altering the injection site. It should be limited to those with advanced endoscopic skills. And training should be lengthened before being certified. Enteryx should be reconsidered for select patients with GERD.

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#### Mesalazine Induced Aplastic Anemia in a Patient with Crohn's Disease

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**Purpose:** A 52 year old woman with a past medical history of Crohn's Disease presented with several months of progressive lethargy, fatigue and one day of bright red blood per rectum. She had lived in Haiti until 1 week prior to admission and she noted that she had been transfused a week before her trip. The patient had been taking 1,000 mg daily of Mesalazine for several years.

She appeared comfortable and physical examination revealed small petechia on her palate and lower extremities. Her initial WBC count was  $3.4 \times 10^9$  and hematocrit was 27%. Her platelet count was  $1 \times 1069/L$ . ANC was 550. Absolute reticulocyte count was  $0.02 \times 10612/L$ . ESR was 90 MMS. PT, PTT and INR were normal. The patient was transfused with platelets. EGD, colonoscopy and capsule endoscopy were unremarkable. Serologic tests for Hepatitis, Parvovirus, CMV, EBV, HIV and PNH were negative. Immunofixation showed no clonal spikes. Bone marrow biopsy revealed a hypocellular marrow. A diagnosis of aplastic anemia was made. The patient was given 1 cycle of cyclosporine and ATG (anti thymocyte antiglobulin) and was discharged on prednisone. Her blood work remains consistent with marrow depression.

The hematological effects of mesalazine are potentially fatal. Initial pharmacological tests in 4000 patients reported no hematological complications. Since then several reports have associated it with severe hematologic anemias as well, including aplastic anemia, neutropenia and thrombocytopenia.

The ages of the patients with aplastic anemia attributed to mesalazine have ranged from 20 to 75 years of age. The dosage and the length of treatment also varied, with one patient experiencing the effect after only 28 days. Patients may present with purpura, bruising, epistaxis or with severe infectious processes precipitated by neutropenia.

The exact mechanism of the aplastic anemia is unclear. Mesalazine may induce immunologic suppression of the of hematopoietic stem cells or effect a direct toxic effect upon those cells. The treatment for mesalazine associated aplastic anemia is a combination of ATG, cyclosporine and granulocyte colony – stimulating factor (G-CSF).

**Conclusion:** Aplastic anemia secondary to mesalazine is a rare but recognized phenomenon. Further studies are needed to identify its frequency. Addition to the side effect profile of mesalazine may affect its choice for therapy of patients with inflammatory bowel disease.

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#### Ulcerative Colitis Diagnosed in a Patient with Venous Thromboembolism

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**Purpose:** Thromboembolic episodes, either in the form of deep venous thromboembolism (DVT) and/or pulmonary embolism (PE), are infrequently observed in inflammatory bowel disease (IBD). The incidence of venous thromboembolism (VTE) in IBD is 3–3.6 times greater than control groups and is one of the serious complications of IBD, associated with high morbidity and mortality. The underlying mechanisms of increased VTE in IBD are multifactorial and still unclear. The infrequent but serious outcome of such IBD complications demands a challenging diagnosis.

A 61-year-old male with unremarkable past medical history, presented to ED, complaining of dyspnea of one month's duration. On admission, patient was noted to have profound anemia with a Hb 8.0 g/dL, unilateral calf tenderness, significant weight loss and heme positive stool. On system review, he related 3 month history of intermittent diarrhea with blood admixture. Subsequently, Doppler US revealed DVT of the left lower extremity. The extensive pulmonary embolism involving left main pulmonary artery was detected on Spiral chest CT. The patient was transferred to intensive care unit, transfused with packed RBCs and started on low molecular weight heparin (LMWH). After improvement of his anemia, a gastrointestinal work up was undertaken due to strong suspicion of possible malignancy. Colonoscopy showed friable edematous and erythematous mucosa, and shallow scattered ulcerations throughout the large bowel from rectum to cecum. Biopsies revealed moderate to severe active chronic pan-colitis, consistent with ulcerative colitis, without evidence of dysplasia. P-ANCA (anti-neutrophilic cytoplasmic antibodies) was elevated and thrombophilia evaluation showed normal homocysteine, protein C, S level, and anti-cardiolipin antibody, but decreased Antithrombin III level. The patient was treated with mesalamine (Asacol) 800 mg po three times a day and mesalamine 4 g retention enema at bedtime. After unremarkable hospital course, the patient was discharged and returned to his country, precluding our follow up.

The case illustrates a patient who was admitted to our hospital with massive PE and DVT, and eventually found to have active UC as an underlying etiology. Albeit uncommon, IBD has been established as a specific manifestation and risk factor which should be included in the differential diagnosis of VTE.

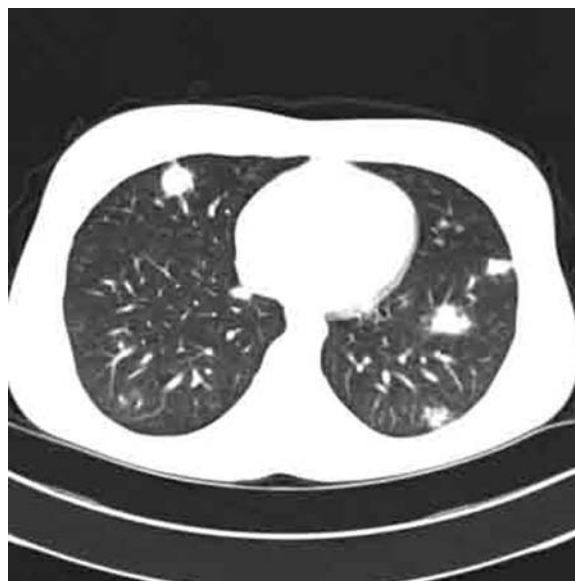
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#### Pulmonary Nodules in Ulcerative Colitis

Thanhtam N. Nguyen, BA\*, Chris Shepela, MD, Patnaik Mrinal, MD. Gastroenterology, Hepatology and Nutrition & General Internal Medicine, University of Minnesota, Minneapolis, MN.

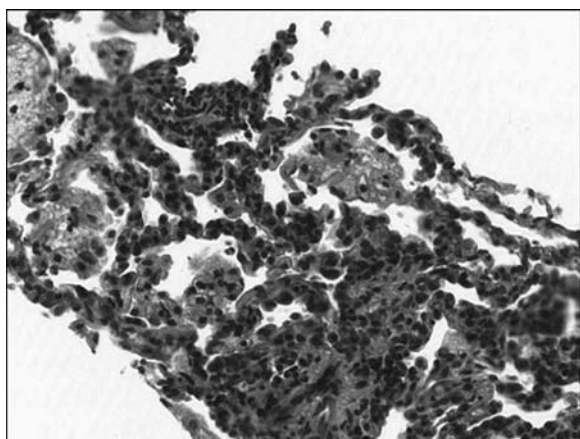
**Purpose:** Inflammatory bowel disease (IBD) exhibits a wide spectrum of pulmonary manifestations. Pulmonary nodules, however, are infrequently reported in the literature as an extraintestinal manifestation (EIM) of IBD. We report a case of a patient who presented with ulcerative colitis (UC) and multiple pulmonary nodules as an EIM of UC.

A 23-yr-old female with a family history of UC was referred to our hospital for acute onset of persistent dry cough and worsening bloody diarrhea. CT of the chest, abdomen, and pelvis revealed multiple bilateral pulmonary nodules, some of which were cavitory in nature, measuring up to 2 cm in diameter and bowel wall thickening involving the entire colon consistent



with pancolitis (Fig. 1). Flexible sigmoidoscopy revealed a diffuse area of congested, friable mucosa in the rectosigmoid region and descending colon. Biopsies showed colonic mucosa with abundant active inflammation and crypt abscesses. CT-guided biopsy of one of the nodules revealed a pattern and distribution consistent with non-specific interstitial pneumonitis (NSIP) (Fig. 2). An extensive autoimmune, immunological, and infectious workup was negative except for a positive IBD serology panel strongly suggestive of UC. The patient was started on IV prednisolone with improvement of pulmonary nodules on repeat CT scan. Repeated chest x-ray at 2 months is back to normal.

To our knowledge, this is the first case of acute UC with pulmonary nodules as the initial presentation. Histologically, pulmonary nodules as an EIM of IBD vary from being necrobiotic, granulomatous, to focal aggregates of lymphocytes. The NSIP pattern observed in our patient's lung biopsy is distinct from what has been reported in the literature and may constitute a new addition to the spectrum of histological patterns seen in pulmonary nodules linked to IBD.[figure1][figure2]

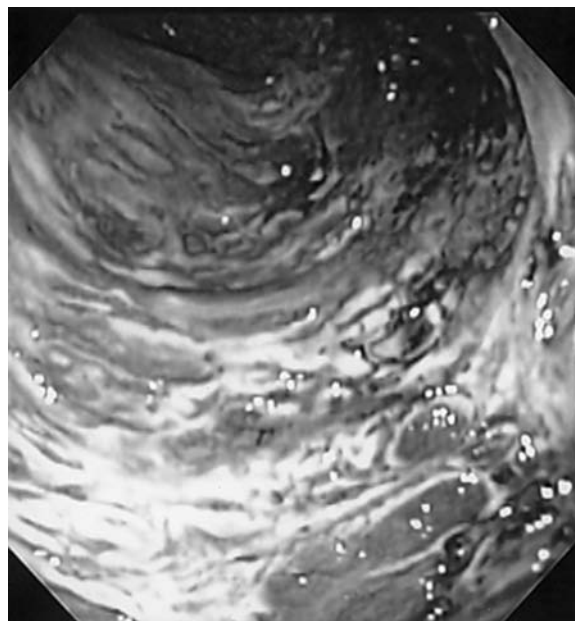


*Isam Daboul, MD\*, Vikas Ghai, MD, Adeel Husain, Srini Hejeebu, DO. Gastroenterology, University of Toledo, Toledo, OH and Medicine, University of Toledo, Toledo, OH.*

**Purpose:** Intestinal perforation as a life-threatening complication of toxic megacolon following non-typhoid Salmonella infection has not been reported in the United States according to current literature reviews. The disease is rapidly progressive, and death may ensue due to septicemia and/or perforation.

**Methods:** A 48-year-old gentleman presented to the ER with bloody, watery stools every hour associated with a crampy abdominal pain that progressively worsened with eating. A week prior, the patient presented to an outlying facility where he was prescribed Dicyclomine and Imodium which did not improve his condition. On this presentation, CT scan revealed multiple air-fluid levels and follow up colonoscopy showed necrotic areas throughout the colon with thick white discharge and ulcers. The patient was started on steroids and Flagyl. The stool was negative for Clostridium Difficile and later grew Salmonella group D isolate found to be susceptible to Ciprofloxacin which was then started. The patient's abdominal distention, pain and discomfort began to resolve. He was started on a clear liquid diet and then discharged on treatment.

**Results:** Two days later, the patient again presented to the ER with worsening abdominal pain. Plain films showed severe colonic distention with free air



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#### Hemochromatosis and Ankle Arthritis

*Gennadiy Bakis, MD, Matthew Baichi, MD\*. Division of Gastroenterology, Hepatology, and Nutr, SUNY at Buffalo, Buffalo, NY.*

**Purpose:** Sixty eight year old male with hypertension, glucose intolerance, hyperlipidemia, obesity and history of severe ankle osteoarthritis was referred to gastroenterology for evaluation of elevated liver enzymes. Prior to evaluation he had a nine year history of bilateral ankle pain and swelling which was investigated with multiple radiological studies showing severe degenerative joint disease. Sedimentation rate and ANA were unremarkable. Ankle pain was treated with non-steroidal agents, COX-2 inhibitors, braces, physical therapy and steroid injections with intermittent minimal improvement. Symptoms of bilateral wrists and shoulder pain were also present but much less prominent. The patient also had chronically elevated transaminases that had been attributed to alcohol use. Viral hepatitis serologies, anti-smooth muscle antibodies, alpha-1 antitrypsin were unremarkable. Ferritin was elevated at 6500, iron saturation 85% and patient was C282Y homozygous. Liver biopsy showed 4+ iron and macronodular cirrhosis. Arthropathy is one of many clinical manifestations of hereditary hemochromatosis. Wrist, shoulder, knee and hip joints are most commonly affected. Our patient's long-standing severe ankle osteoarthritis is rare manifestation of hereditary hemochromatosis.

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#### Toxic Megacolon with Perforation: A Complication of Salmonella Colitis in the U.S.

under the diaphragm which suggested toxic megacolon with perforation. The patient then underwent a total colectomy with ileostomy.

**Conclusion:** Dicyclomine and Loperamide should not be used in cases of dysentery as it may predispose to toxic megacolon. Identification of patients with toxic megacolon associated with non-typhi *Salmonella* infections is important as they are at risk for further intestinal perforation. Early effective fluid resuscitation, antibiotics, steroids and rectal tube insertion may be helpful to prevent the occurrence of intestinal perforation.[figure1][figure2]

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#### A Case of Interferon-Induced Anti-Jo1 Positive Polymyositis with Pulmonary Fibrosis

Matthew B. Chandler, MD, David L. Jager, MD, Mary Reyes, MD, Marie L. Borum, MD\*. *Gastroenterology, George Washington University, Washington, DC.*

**Purpose:** Interferon therapy for hepatitis C is rarely complicated by the onset of autoimmune diseases. Thyroid disease, hemolytic anemia and TTP are better known autoimmune diseases complicating interferon therapy. We present a case of anti-Jo1 positive polymyositis with pulmonary fibrosis induced by interferon therapy.

A 54-year old female with hepatitis C and biopsy consistent with mild activity and mild fibrosis was treated with pegylated interferon and ribavirin. After starting therapy, she complained of flu-like symptoms. Four weeks later, she complained of worsening flu-like symptoms, shortness of breath and weakness in her arms and legs prompting admission to the hospital. At admission, her blood pressure, pulse and temperature were normal. She was dyspneic with increased work of breathing. On exam, she had bilateral coarse breath sounds and weakness in the proximal muscle groups in all extremities. Labs at admission were ALT93, AST115, Alkp144, TB0.2, Alb2.8, CPK2637, Aldolase33.8, ANA<1:40, dsDNA<30, C4<8, C3<9, RF14, and ESR70. Anti Jo1 was positive. SSA, SSB, pANCA, anticardiolipin, ASMA, and AMA were negative. Chest x-ray showed bilateral interstitial infiltrates. The patient underwent bronchoscopy with biopsy demonstrating interstitial organizing pneumonitis and chronic bronchitis. Pulmonary function tests demonstrated moderate chest restriction with reduced DLCO to 30% of predicted. Clinical presentation suggested a diagnosis of anti-Jo1 positive acute polymyositis with interstitial pneumonitis. This constellation of clinical features comprises the antisynthetase syndrome. Interferon therapy was discontinued and the patient was treated with cyclophosphamide and prednisone. She had gradual improvement in her weakness and pulmonary function. The serum aldolase and creatine phosphokinase levels returned to normal.

Interferon therapy is rarely complicated by the development of autoimmune diseases. There have been few reports of acute polymyositis with pulmonary fibrosis associated with interferon therapy. The presence of anti-Jo antibody in patients with acute polymyositis is associated with the development of pulmonary fibrosis. An association between Anti-Jo1 positive polymyositis and hepatitis C has been previously described in patients without exposure to interferon therapy. Because of the temporal relationship between interferon therapy and the development of symptoms of this rare disease, the patient presents with interferon-induced antisynthetase syndrome.

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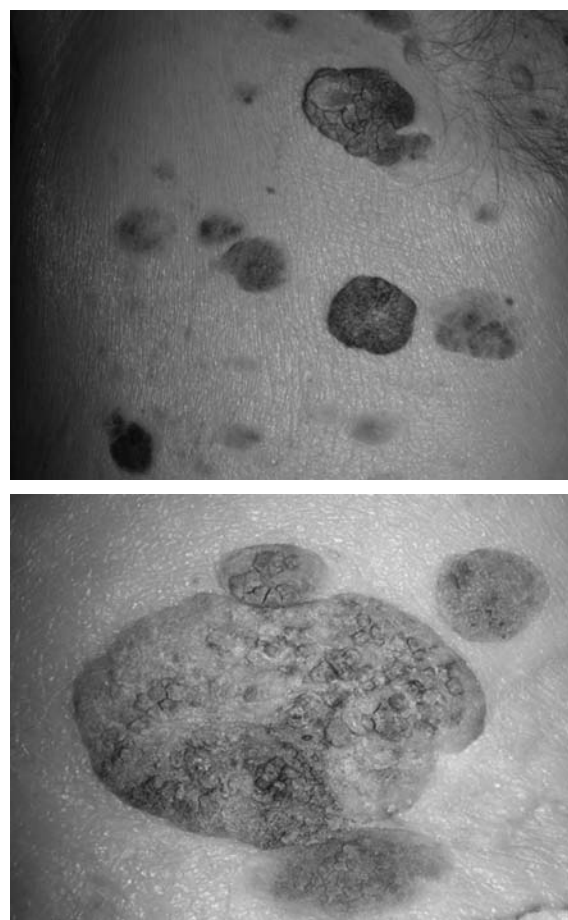
#### Sign of Leser-Trélat

Audrey H. Calderwood, MD, Robert C. Lowe, MD\*. *Gastroenterology, Boston Medical Center, Boston, MA.*

**Purpose:** An 86 year old man complained of abdominal discomfort and early satiety. He noted an increase in size and number of lesions on his right flank that had been stable for decades prior. On exam, he was deeply jaundiced with an enlarged, firm epigastric mass that was tender to palpation. There were multiple, lichenified lesions on his right flank consistent with eruptive seborrheic keratoses (Figs. 1, 2). Laboratory evaluation showed a

total bilirubin of 17.9 mg/DL, alkaline phosphatase of 987 U/L. Computed tomography showed a large mass in the porta hepatitis with replacement of liver parenchyma by tumor and compression of the common bile duct. Liver biopsy revealed poorly differentiated adenocarcinoma of bile duct origin. Consideration was given to ERCP with palliative common bile duct stent but the patient refused. He was also evaluated by oncology but declined further treatment. One month after diagnosis, he was referred for hospice care.

The sign of Leser-Trélat was first described in 1890 and is characterized by the abrupt appearance of multiple seborrheic keratoses that rapidly increase in size and number. This paraneoplastic syndrome is seen most often in adenocarcinoma of the gastrointestinal tract (stomach, colon, liver, pancreas), but can also occur in breast and lung cancer, renal cell carcinoma, lymphoma and leukemia. This cutaneous finding may be the first sign of visceral malignancy and should prompt further investigation.[figure1][figure2]



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#### The Buried Bumper Syndrome in Children

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**Purpose:** Case #1: A 10 month old former 25 week preterm newborn with a history of chronic lung disease and gastroesophageal reflux (GER). At 2 months a Nissen fundoplication with surgical gastrostomy tube (GT) was performed due to severe GER. The infant consumed adequate calories by mouth and initially never required use of the GT. Due to worsening respiratory issues he underwent a video swallow study which revealed aspiration.

Feeds were discontinued by mouth, replaced by GT feedings. Abdominal distention and fussiness were noted with GT use. A fluoroscopic GT study showed the GT balloon to be within the gastric antrum with partial gastric outlet obstruction. This led to surgical revision of the GT with a 14 French mushroom tube. Four weeks after the revision he presented with fever. A fluoroscopic study revealed a small gastrocutaneous fistula tract adjacent to the GT site with edema. Antibiotics were started and an esophagogastro-duodenoscopy (EGD) performed. The endoscopic images demonstrated a "buried bumper" with incomplete intragastric visualization of the gastrostomy device. The GT was removed.

Case #2: A 7 year old with Hurler's syndrome had a Gastro-jejunostomy (GJ) tube placed at 1 year of age due to concern of aspiration and poor oral feedings. He presented with a 3 week history of redness and bulging around the GJ tube site and swelling with use of the GJ tube. Around the site there was an 8 cm circumferential area of erythematous, indurated tissue. An ultrasound of the area revealed a 4 cm balloon with surrounding edema. Subsequently an EGD demonstrated the balloon buried completely under granulation tissue. The balloon was deflated and the GJ tube was removed successfully.

**Conclusion:** Buried bumper syndrome (BBS) is caused by internal migration of the internal bumper into the gastric wall usually due to excessive tension applied to the tube. The internal bumper may become completely overgrown by gastric mucosa and is usually a late complication. Most reported cases have been in adults. Prevalence ranging from 1.5% to 6.1%. It may present as increased leakage around the site, immobility of the catheter, resistance of infusion, or abdominal pain. Once diagnosed the solution is removal of the tube. Failure to recognize this complication may result in GI bleeding, gastric perforation, peritonitis, and even death.

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#### **Fine Needle Aspiration Biopsy (FNAB) of a Rare Case of Malignant Seeding of Percutaneous Endoscopic Gastrostomy (PEG) Tract: Direct Implantation during PEG Insertion or Seeding Via Hematogenous Spread?**

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**Purpose:** PEG insertion is routinely performed in patients with potentially obstructive head and neck cancers, during surgery for tracheostomy placement or prior to definitive radiation therapy. We describe a case of one such patient who developed metastasis at the gastrostomy stoma possibly as a result of PEG placement. The diagnosis was made by FNAB.

A 56 year-old African American woman with a prior history of ethanol and tobacco abuse presented with the complaints of dysphagia and odynophagia. She was diagnosed with cT3N2bM0 Squamous Cell Carcinoma (SCC) of the right aryepiglottic fold.

A PEG tube was placed to relieve her symptoms and to provide a mechanism for nutrition and hydration during subsequent therapy. A Pull technique was employed for the procedure. Radiation and chemotherapy were then administered. Later, she underwent neck dissection and six out of twenty three lymph nodes were found positive for carcinoma. She was also found to have venous involvement by SCC.

Approximately seven months after the placement of the PEG tube, localized swelling was noted around the gastrostomy site. A FNAB was performed around the opening which revealed SCC, and was found similar to the patient's previous surgical neck dissection and biopsy lesion.

A CT scan revealed extension of the lesion across the abdominal wall into the stomach. EGD showed the tumor mass in the gastric wall. The patient expired approximately nine months following her initial diagnosis of SCC. Although PEG placement for head and neck cancers is common, the metastasis to a PEG tube exit site is extremely rare. While direct implantation

with a variable-sized initial tumor burden may explain many of the cases of PEG site metastasis, it is controversial whether this metastasis occurs as a result of direct implantation of the malignant cells during PEG placement or from vascular seeding of tumor cells at the vulnerable incision site. This case emphasizes the importance of FNAB in diagnosis of such tumor metastasis.

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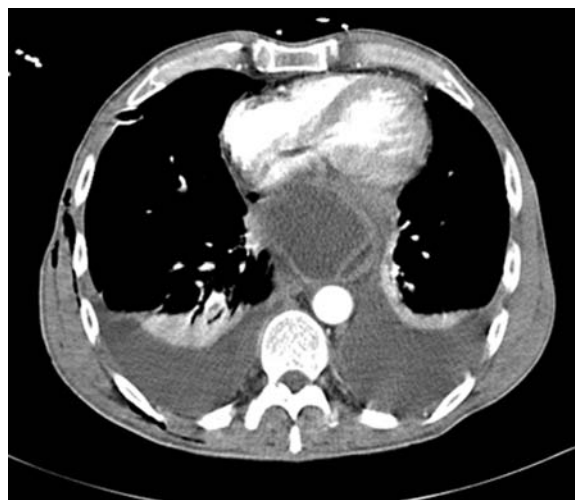
#### **A Pancreatic Pseudocyst Presenting as Dysphagia and Review of the Literature**

Sandra M. Jara, MD, Francene Martin, MD, Patrick Brady, MD\*. Division of Digestive Diseases, University of South Florida, Tampa, FL.

**Purpose:** Pancreatic pseudocysts are a common complication of acute and chronic pancreatitis. Very rarely a pseudocyst may extend into the mediastinum by way of the esophageal or aortic hiatus and present with dysphagia. This abstract reports an unusual case of dysphagia as the leading symptom in a patient with chronic pancreatitis.

**Methods:** A 46 y.o. male with a history of chronic alcoholic pancreatitis and chronic pain syndrome presented with solid food dysphagia and weight loss. A CT scan of the chest revealed a large, lobulated 10 cm × 16 cm fluid collection within the posterior mediastinum which displaced the liver, heart, IVC, and left atrium (Fig. 1). An abdominal CT scan showed a pancreatic pseudocyst which communicated with the retrohepatic fluid collection and extended into the inferior portion of the posterior mediastinum through the diaphragmatic hiatus. An ERCP with sphincterotomy was performed to evaluate communication of the pseudocyst with the pancreatic duct; however, successful cannulation of the pancreatic duct was not achieved. A 2D cardiac echo was performed to evaluate potential cardiac compromise from cystic structure without evidence of cardiac tamponade seen. The patient was followed by GI, cardiothoracic and trauma surgery services during his hospitalization. Once his nutrition was appropriate he underwent a pancreatic cystogastrostomy and did well following the surgery.

**Conclusion:** A mediastinal pancreatic pseudocyst is a rare and potential cause of dysphagia. Pancreatic pseudocysts should be considered in the differential diagnosis of mediastinal cystic lesions.[figure1]



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#### **An Unusual Case of Dysphagia Caught on 3-D CT**

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**Purpose:** 64 year old female with chronic cough, which has gotten worse in last 1.5 years and failed treatment with inhalers for presumed asthma and PPI for presumed GERD. Patient started to have progressively worsening

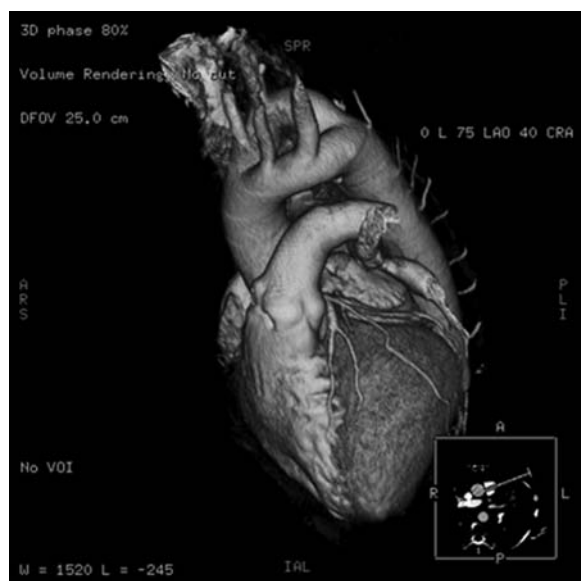
cough after almost every meal. She had mild dysphagia to solids more than liquids for unknown period of time and denied any abdominal pain, weight loss, melena or hematochezia. Patient's past medical history included hypothyroidism, hypertension, thymectomy, tonsillectomy/adenoidectomy and cholecystectomy. Physical exam revealed normal neck, abdominal, and pulmonary exams except for the fact that the patient had minimal cough during the exam.

Video fluoroscopic exam showed circumferential narrowing of the esophagus at the level of the aortic arch. Endoscopy via naris showed a ring in the cervical esophagus at 30 cm from the nasal vestibule. 3-D CT scan revealed double aortic arch as the reason for the patient's symptoms (see figure). Patient had surgical division of the left aortic arch with improvement of her symptoms.

Early in embryonic morphogenesis, 6 pairs of pharyngeal arch arteries develop. Normally, left fourth arch becomes the aortic arch and the right fourth arch contributes to the innominate artery. Vascular rings are formed when this process of regression and persistence does not occur normally, and the resulting vascular anatomy completely encircles the trachea and esophagus. Pathogenesis is unknown. Among patients with vascular rings, those with double aortic arch present earlier than those with other anatomic variations. Esophageal symptoms include emesis, choking, or dysphagia and are more common in older infants and children. Occasionally, patients may reach older childhood or adulthood before developing persistent or progressive symptoms of dysphagia, respiratory symptoms, or both.

Chest radiograph can show indentation of the tracheal air column. Bilateral indentation of the esophagus is observed on the AP view of barium esophagram and posterior indentation on the lateral view. MRI and CT are the best single imaging studies.

Treatment is surgical division of the ring to relieve compression of the trachea and esophagus achieved by dividing the minor arch through an ipsilateral thoracotomy.[figure1]



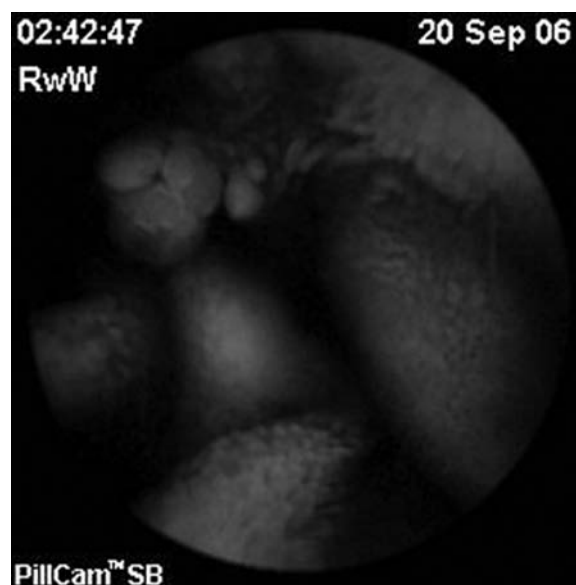
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### Jejunal Varices Detected on Capsule Endoscopy as the Cause of Recurrent GI Bleed

Brian S. Lim, MD, John Rabine, MD, Surinder K. Mann, MD\*. Gastroenterology & Hepatology, UC Davis Medical Center, Sacramento, CA; Gastroenterology, Sacramento VA Medical Center, Mather, CA and David Grant USAF Medical Center, Travis Air Force Base, CA.

**Purpose:** We present a case of a 45 year old male with history of abdominal gunshot wound in 1980's and small wedge resection of the liver for laceration. Patient developed GI hemorrhage in 2004, and workup revealed hepatic hemangiomas as the likely source. Patient reportedly had embolization with coils without success and continued to have bleeding episodes. Several months later, he had right hepatectomy and Roux-en-Y hepaticojejunostomy since hepatic hemangiomas were still the suspected etiology of his GI bleed. However, he continued to have bleeding. At some point around this time, he was diagnosed with portal vein thrombosis and portal hypertension, though the exact details of this diagnosis are not known. He had extensive evaluations including multiple endoscopies at two teaching medical centers with no definitive conclusion. Patient was then seen at a different hospital for a massive GI hemorrhage in 2006. During that admission, EGD/enteroscopy showed grade I esophageal varices, questionable gastric varices, and mild portal gastropathy. Colonoscopy showed mild portal colopathy and small internal hemorrhoids. Tagged RBC scans and angiogram did not locate the source of bleed. CT scan suggested the possibility of varices within jejunum. This is when the patient was referred to our facility for capsule endoscopy, which demonstrated four clusters of varices in jejunum with fresh blood approximately 2 hours and 40 minutes into the study. The patient was not a candidate for TIPS because of his extensive portal vein thrombosis and underwent surgery for splenorenal shunt with an associated splenectomy. He currently remains stable without any further episodes of gastrointestinal bleeding.

Bleeding from jejunal varices is an uncommon manifestation of portal hypertension. Recently, capsule endoscopy has been used in the workup of obscure-overt GI bleed as in our case. Our case represents one of the first reports of jejunal varices detected on capsule endoscopy as the cause of GI hemorrhage.[figure1]



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### A Case of Thyrotoxic Crisis Leading to Fulminant Hepatic Failure

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**Purpose:** The goal of this clinical vignette is to illustrate the relationship between thyrotoxicosis and liver failure.

**Methods:** Hepatology was consulted on a patient admitted to Cardiology at a university medical center.

**Results:** A 49 year old male, without known medical history, presented to the Emergency Department complaining of swelling and shortness of breath. Associated symptoms included anxiety, weight loss, cough, and diarrhea. The patient's family history was significant for a "thyroid problem." Physical examination revealed exophthalmos, jugular venous distension, irregularly irregular tachycardia, bibasilar rales, abdominal distension, and bilateral lower extremity pitting edema. The patient's initial laboratory evaluation revealed AST of 81, ALT of 55, alkaline phosphatase of 249, total bilirubin of 2.5, INR of 1.7, free T<sub>3</sub> of 1605, and free T<sub>4</sub> of 7.0.

The patient was dosed with methimazole, as the clinical picture met criteria for thyrotoxic crisis. Subsequently his transaminases increased to greater than 25 times the upper limit of normal. Total bilirubin, alkaline phosphatase, and INR also increased further. Apheresis was utilized, given the patient's apparent inability to tolerate methimazole. Follow-up thyroid hormone levels were improved as were the transaminases, despite mental status changes and worsening congestive heart failure.

Thyroid hormone levels again began to increase despite additional sessions of plasmapheresis; therefore, the patient was redosed with methimazole. The transaminases continued to decrease, but thyroid hormone levels improved only slightly. Given the patient's multisystem organ failure, his sister opted for comfort care. The patient passed away on the eighth day of hospitalization.

**Conclusion:** The patient suffered from fulminant hepatic failure secondary to thyrotoxicosis. An increase in transaminases has been reported in 25–40% of patients in thyroid storm; however, there are few reports of thyrotoxicosis presenting with fulminant hepatic failure. It is difficult to establish which features of thyrotoxic liver injury are of multifactorial etiology. In this patient methimazole may have been a contributing factor. Rare cases of methimazole-induced liver injury have been reported, but are usually cholestatic in nature and occur over a longer time course. In the vast majority of cases, the hepatic abnormalities associated with hyperthyroidism are reversible following early recognition and treatment of the disorder.

## 653

#### Azathioprine Induced Sweets Syndrome in a Patient with Crohn's Disease

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**Purpose:** Sweets syndrome, or acute febrile neutrophilic dermatosis, is a condition typified clinically by the abrupt onset of fever, leukocytosis, and painful red papules or plaques. Histologic examination shows dense neutrophilic infiltrates. It may be associated with inflammatory, infectious, or neoplastic diseases as well as multiple medications.

Our patient, a 31 year old Kuwaiti man, presented for evaluation of a 10 year history of fistulizing Crohn's colitis, treated with chronic steroids. Azathioprine (AZA) had been trialed seven years prior, but was discontinued after he developed a skin infection within a week. At initial evaluation, setons were placed in two peri-rectal fistulas and AZA was again started at 100 mg per day. His chronic prednisone at 10 mg a day was continued with anticipation of a future taper. Six days later, the patient developed fever and tender erythematous plaques over the dorsum of his hands and feet as well as his face. The patient was admitted to hospital, where his temperature was 39.2 C, pulse 104, and blood pressure 98/58. White blood cell count and C reactive protein were elevated at  $23.4 \times 10^9/L$  and 19.4 mg/dL respectively. Broad spectrum antibiotics for a presumptive cellulitis were begun. Despite this, the patient continued to be febrile over the next three days. His rash progressed, with pustules developing over his previous plaques. A skin biopsy was taken from one such lesion, from which cultures and stains were negative for infection. Histology showed neutrophilic infiltration of the stratum corneum and microabscesses. Given the absence of infectious agents and characteristic biopsy findings, Sweets syndrome was diagnosed. Antibiotics and AZA were stopped, and prednisone was increased to 40 mg per day. He promptly defervesced and the skin lesions began to improve within two days.

Complete resolution, after desquamation of the affected areas, was seen at three weeks.

Sweets syndrome is a rare complication of inflammatory bowel disease, with fewer than 50 cases reported in the literature. A single case of possible drug induced Sweets has been reported in association with AZA administration, but the association is complicated by the presence of underlying IBD. However, given the temporal association of AZA dosing and symptoms in this episode, as well as seven years ago, this most likely represents a case of drug induced Sweets syndrome.

## 654

#### Case of Chronic Hepatitis C Presenting with Right Axillary Lymphadenopathy

Biju K. Alex, MD, Roshan M. Bashir, MD\*. *Department of Medicine, Washington Hospital Center, Washington, DC.*

**Purpose:** Chronic hepatitis C is the most common cause of chronic liver disease. Most patients with chronic infection are usually asymptomatic or have mild nonspecific symptoms such as fatigue, myalgias, arthralgias, weakness, and weight loss. Extrahepatic manifestations have been associated with chronic hepatitis C infection. We present an unusual case of a patient with hepatitis C presenting with right axillary lymphadenopathy.

**Case Presentation:** This is a 52 year old African-American male with history of hepatic C who noticed an enlarging mass under his right armpit for 2 1/2 months. He reports no night sweats, fevers, fatigue or weight loss. He denied any abdominal pain and review of system was otherwise negative. Physical exam was notable for 6 cm area of adenopathy in his right axilla. All other areas including supraclavicular, cervical, groin and left axillary were negative for adenopathy. Abdominal exam was nontender without hepatosplenomegaly. Liver enzymes including AST, ALT, Alk Phos were normal. The right axillary lymph node was excised. Pathology revealed florid follicular hyperplasia (Fig. 1). There was no evidence of Reed-Sternberg cells or variants. Immunostain for hepatitis C virus showed multiple foci of scattered positive intranuclear staining of macrophages and lymphocytes. The final diagnosis was florid reactive follicular hyperplasia associated with hepatitis C viral infection.

**Conclusion:** To our knowledge, this is the first case of a patient with chronic hepatitis C presenting with right axillary adenopathy associated with the disease.

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#### Carcinoid Tumor of Small Bowel and Colonic Adenocarcinoma, a Concurrent Occurrence in a 77 Year Old Male

Alka Farmer, MD, Howard Benn, MD\*. *Internal Medicine, St. Joseph Regional Medical Center, Paterson, NJ.*

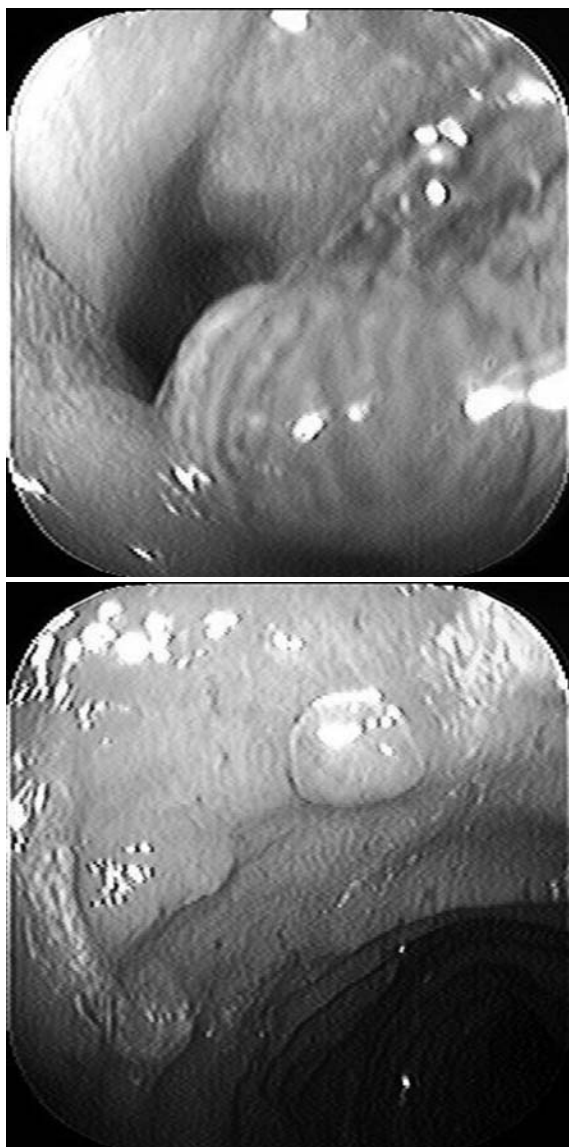
**Purpose:** Carcinoid tumors are the most frequent GI neuroendocrine tumors. It is thought that carcinoid tumors and adenocarcinoma arise de novo from the same pluripotent stem cell, however the incidence of adenocarcinoma is higher. We present a case of a patient presenting with synchronous carcinoid tumor and colon adenocarcinoma, 25 year after resection of a primary small bowel carcinoid tumor.

**Methods:** A 77 year old male presented with 2 month complaint of flushing, nausea, vomiting, diarrhea and weight loss (25 lb). His medical history was significant for small bowel resection for a primary carcinoid tumor in 1981, with complete resolution of obstructive and neuroendocrine symptoms. Physical examination revealed hypertension, cutaneous flushing, generalized abdominal tenderness and ascites. CT scan demonstrated bowel obstruction.

Subsequent colonoscopy revealed a polyp in the sigmoid colon and an obstructing friable splenic flexure mass. Labs revealed elevated serotonin -605, Chromogranin A- 300 and normal CEA. A subtotal colectomy with ileorectal anastomosis was performed. Small bowel pathology was consistent with carcinoid tumor. Colon pathology was significant for typical carcinoid with

concurrent well differentiated adenocarcinoma. Chemotherapy was initiated. Patient died within one month due mainly to metabolic complications associated with short bowel syndrome.

**Conclusion:** GI carcinoids, especially those arising within the small bowel have been associated with increased incidence of synchronous and metachronous *de novo* adenocarcinoma. However, because of the great disparity in tumor cell growth rates, carcinoid tumors requires 40 years doubling time, compared to adenocarcinoma which requires 17.8 years, synchronous presentations are rare. The current patient may represent a *de novo* carcinoid/adenocarcinoma synchronicity or recurrent carcinoid/adenocarcinoma pathology.[figure1][figure2]



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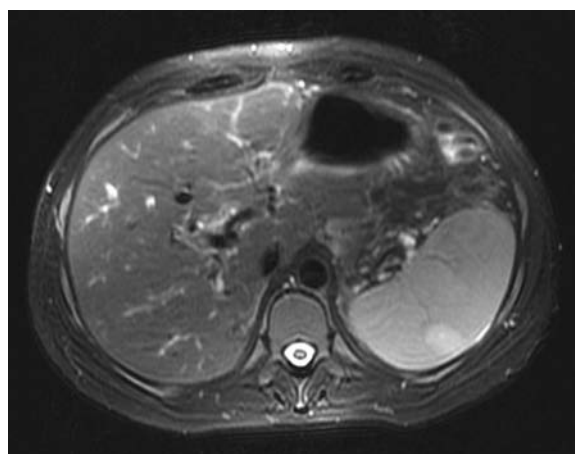
#### Multifocal Splenic Steatosis in End Stage Cholestatic Liver Disease

Jeffrey Tang, MD, Chetan Pai, DO, Stuart C. Gordon, MD\*. Internal Medicine, Division of Gastroenterology, Henry Ford Hospital, Detroit, MI.

**Purpose:** The multifocal variant of diffuse hepatic steatosis frequently mimics metastatic disease on imaging studies, but similar condition involving the spleen is not described. We report a case of multifocal splenic steatosis masquerading as primary splenic lymphoma.

**Methods:** A 47-year old man with end stage primary sclerosing cholangitis underwent orthotopic liver transplant (OLT) evaluation and was found at routine magnetic resonance imaging (MRI) to have multifocal splenic lesions. His past history included ulcerative colitis and hyperlipidemia, with recent weight loss and muscle wasting. Physical examination showed jaundice, hepatosplenomegaly, and diffuse xanthelasmas. Laboratory data showed a total cholesterol of 1,311 mg/dL and an low density lipoprotein of 1,238 mg/dL. MRI showed four hyperintense enhancing splenic masses ranging in size from 2.6 cm to 3.5 cm, highly suspicious for lymphoma. Prior to formal OLT listing the patient underwent diagnostic splenectomy. Microscopically the focal lesions showed infiltration of red and white pulp consistent with nodular and diffuse lipidosis without evidence of malignancy.

**Conclusion:** Splenic fat infiltration may result from intravenous fat emulsions, but its occurrence in hyperlipidemic liver disease has not been previously described. In cholestatic disorders, high serum levels of lipoprotein X require an intact reticuloendothelial system (RES) for removal from circulation. We speculate that in this patient with advanced cirrhosis, his splenic RES may have led to disordered lipid deposition. The MRI appearance in this case was not consistent with usual steatosis, thus the aberrant lipoprotein of advanced cholestasis may have created an atypical imaging finding. In the setting of advanced cholestatic liver disease with hyperlipidemia, knowledge of the entity of focal splenic fat could broaden the differential diagnosis of splenic lesions.[figure1]



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#### An Unusual Case of Right Upper Quadrant Pain

Christopher B. Keller, DO, Jorge L. Herrera, MD\*. Internal Medicine, University of South Alabama, Mobile, AL and Division of Gastroenterology, University of South Alabama, Mobile, AL.

**Purpose:** The differential diagnosis of nausea, vomiting and right upper quadrant pain is broad. We present a case presenting with an unusual cause of these symptoms.

A 47 year old female presented with back and chest pain after falling in the shower approximately 2 hours prior to arrival. The pain was worse with deep inspiration. She reported a recent history of subjective fevers, chills, nausea, vomiting and decreased appetite. On exam vital signs were stable and she was afebrile. Breath sounds were decreased at the right base, and dullness to percussion with decreased fremitus was noted. Bowel sounds were normal, hepatomegaly with tenderness to palpation in right upper quadrant was present. Laboratory data revealed hemoglobin of 11.2 g/dL, white blood cell count of 8,900/mcL with 17% bands, sodium 130 meq/dL, albumin 2.8 g/dL, INR 1.2, and PTT 39 sec. Chest x-ray showed elevated right hemidiaphragm (Fig. 1). CT scan revealed an enlarged liver with numerous cysts throughout and a single left renal cyst (Fig. 2). Two dominant cysts were accessible for drainage with ultrasound guidance. Despite high fevers during her stay, no positive cultures were obtained. The patient was treated with empiric



antibiotic therapy for the duration of her stay with resolution of fever and leukocytosis. She was discharged on amoxicillin clavulanate for 6 weeks. Patient has remained afebrile and asymptomatic in follow up visits.

Polycystic liver disease (PCLD) is an inherited disease that was once thought to be only associated with polycystic kidney disease. It is now known to be a distinct genetic syndrome. Isolated PCLD is usually asymptomatic and under diagnosed. When symptoms develop in these patients it's usually due to mass effect of large cysts or from cysts infection or rupture. The liver usually remains functionally normal, although portal hypertension may develop. Clinical presentation includes abdominal distention, early satiety, dyspnea, and back pain. Fever and chills are associated only with infected cysts. Valvular and vascular abnormalities are some of the extra hepatic manifestations of PCLD.

Asymptomatic patients should receive no treatment. Patients with infections need draining of the infected cyst and antibiotic therapy. Complications from portal hypertension may require a liver transplant.

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### Liver Transplantation for Infliximab-Induced Fulminant Hepatic Failure

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**Purpose:** Infliximab (Remicade®) is a chimeric monoclonal antibody that binds TNF $\alpha$  and is indicated for Rheumatoid arthritis, Crohn's disease, Ankylosing spondylitis, Psoriatic arthritis, and Ulcerative colitis. Potential adverse effects of Infliximab include infusion reactions and risk of serious infections including tuberculosis. Hepatotoxicity has recently been recognized as a potentially serious adverse effect of Infliximab. We report a case of Infliximab-induced fulminant hepatic failure resulting in orthotopic liver transplantation.

**Methods:** A 53 year old African-American female with Rheumatoid arthritis was initially treated with systemic steroids and methotrexate. She had no history of chronic liver disease and all baseline laboratory studies, including liver panel, were within normal limits. Since she continued to remain symptomatic, methotrexate was stopped and infliximab was initiated. She received four infusions over 12 weeks and presented two weeks after the fourth infusion with progressively worsening jaundice. Infliximab was then discontinued. Laboratory studies revealed: Total Bilirubin 4.3 mg/dl, AST 1797 U/L, ALT 1807 U/L, Alkaline phosphatase 193 U/L, PT/INR 15.3/1.6. Since her laboratory studies continued to worsen, a liver biopsy was performed. This revealed marked bile duct damage, diffuse ballooning degeneration of hepatocytes with lobular disarray and cholestasis with a scattered mixed inflammatory infiltrate. Over the course of the next several days, there was continued deterioration of hepatic synthetic function (Total Bilirubin 19.9, PT/INR 27.7/3.1) with onset of hepatic encephalopathy. She was then listed and underwent orthotopic liver transplantation ten weeks after the last infusion of infliximab. The explant showed submassive necrosis with large areas of hepatocyte dropout, collapse of hepatic lobules and marked bile ductular proliferation with cholestasis. She had an uneventful post-operative course and remains well six months after transplant.

**Conclusion:** The precise mechanism of hepatotoxicity of TNF $\alpha$  inhibitors remains unclear. Unlike many of the reported cases of hepatotoxicity related to use of Infliximab, our patient was not on concomitant therapy with immunosuppressants or other potentially hepatotoxic medications. Our case highlights the potential for severe cholestatic liver injury from Infliximab. Clinicians should be aware of this possibility with prompt discontinuation of the drug in patients who develop progressive liver test abnormalities.

## 659

### Carcinoid Liver Metastasis "Cured" by Cholecystokinin (CCK)

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and Department of GI Medicine and Nutrition, UT MD Anderson Cancer Center, Houston, TX.

**Purpose:** Octreotide scintigraphy is widely used in imaging of neuroendocrine tumors which express a high rate of somatostatin receptors. It is considered to be highly sensitive and specific in diagnosing hepatic metastasis of carcinoid tumors. We here by present an unusual cause of false positive hepatic metastasis that can potentially be overlooked.

A 52 year old female underwent an EGD for work up of dyspepsia. EGD revealed a nodule in the duodenum the biopsy of which revealed it to be a carcinoid tumor. An EUS revealed the tumor to be localized to the deep mucosa/submucosa area with an intact muscularis propria. EMR was done with histopathology of the resected tumor confirming it to be carcinoid. Octreotide scintigraphy (In-111 Octreotide), done to evaluate for the presence of metastatic disease revealed a 3.5 cm area of increased activity in the liver compatible with hepatic metastasis where as Computerized Tomography (CT) scan and Magnetic Resonance Imaging (MRI) scans of the liver did not show any abnormality. Due to this discrepancy and since there was a case report describing intense gall bladder concentration that caused diagnostic confusion (Kipper and Krohn 1997), it was decided to repeat the Octreotide scintigraphy with cholecystokinin (CCK) administration during the test. A repeat Octreotide scan before the administration of CCK showed findings similar to previous scan (presence of the 3.5 cm hot spot in liver). CCK was administered to empty the gall bladder. The area was found to diminish in activity within minutes after CCK was administered and was totally absent in images obtained 24 hours later. The scan was read as normal.

Traditionally, presence of Octreotide tracer in gall bladder was considered to be diagnostic for presence of neuroendocrine tumors since only 2% of In-111 Octreotide is cleared through hepatobiliary excretion. But there have been at least five published reports of false positive octreotide scans that were interpreted as normal after repeating the scan following a fatty meal. Awareness of this potential source of diagnostic confusion is very important in interpreting hepatic metastasis of neuroendocrine tumors and findings should be correlated with cross sectional imaging. Since gastroenterologists/hepatologists are involved in the care of patients with gastrointestinal carcinoid tumors we felt it was important to present this case of "hepatic metastasis" cured by CCK.

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### An Unusual Cause for Rectal Mass

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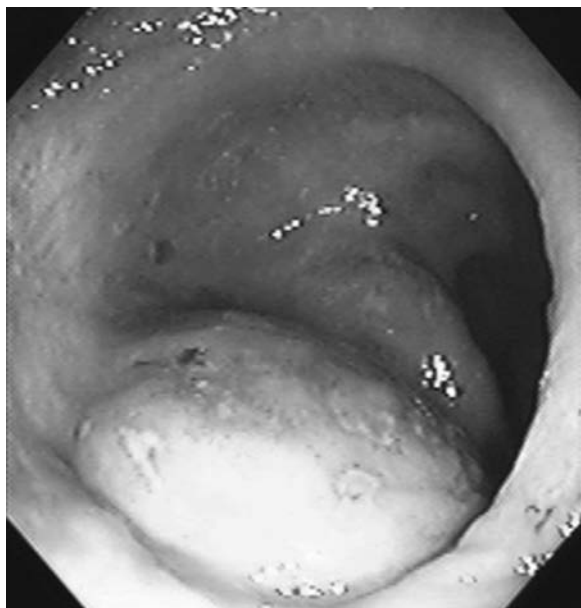
**Case Report:** A 77 yo Female was found to have a rectal mass on evaluation of occasional rectal bleed after bowel movement. She had a long history knee arthritis (treated occasionally with non-steroidal) and dyspepsia (resolved on over the counter antacids). Physical exam was unremarkable except for the rectal lump felt on digital exam, with no inguinal lymph nodes appreciated. She had positive stool guaiac (heme-occult) testing. Lab test did not show anemia. Colonoscopy showed a large non-ulcerated 3 x 3 cm firm rectal mass noted 8 cm into the rectum. The remainder of the colon showed diverticular disease and internal hemorrhoids. Biopsies showed diffuse infiltration by small to medium sized atypical lymphoid cells. Immunohistochemical staining and flow cytometric analysis showed a monoclonal lambda B-cell population and CD markers highly indicative of Extranodal Marginal B-cell lymphoma of MALT type. Imaging showed bilobed rectal hypervascular mass, which is continuous with the posterior wall of the rectum. No evidence of metastasis. PET CT confirmed the findings. Upper endoscopy showed gastritis and the presence of H pylori. This was successfully eradicated (C-14 urea breath test negative), but the rectal tumor did not regress.

MALT lymphoma constitutes 5% of all NHL. The stomach is the most common site, but it can also be found in the lung, thyroid, breast, orbit, skin & soft tissues. Systemic symptoms rarely occur. These tumors are slow growing and metastasis occurs late. Localized lymphomas of the stomach respond



well to H pylori therapy while non-gastric ones can be cured with local therapy (surgery or radiation). These options were offered to the patient and she opted for local radiation. She received a total of 45 Gy of 3D conformal external beam radiation therapy. Repeat colonoscopy and PET scans for 2 years have not shown recurrence, and the only complaint has been occasional rectal bleed from newly developed angiodysplasia which were managed by argon plasma coagulation.

This is only the third case report of primary MALT lymphoma of the rectum here in the US and we describe the role of non-surgical approach in this case (unique to ours).[figure1]



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#### A Rare Case with a Rare Presentation

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**Case:** A 71-year-old male presents to his primary complaining of left-sided low back pain radiating to the mid-abdomen. CT scan showed a 5 cm soft tissue mass. Subsequent exploratory laparotomy with biopsies leads to a diagnosis of sclerosing mesenteritis. The patient was discharged following G-tube decompression. He remained relatively asymptomatic until one year later when he developed worsening left-sided low back pain radiating to the epigastrium. The pain is unrelenting, intensified postprandially and associated with nausea. He finds no relief with conservative therapy. Physical exam shows normal active bowel sounds, and a tender mid-epigastric palpable mass. Abdominal x-ray does not demonstrate bowel obstruction. CT scan reveals a calcified mass now measuring 10 cm encasing portions of the superior mesenteric artery. Concern for mesenteric ischemia is entertained, and a selective superior mesenteric angiogram is performed. Results yield an encased ileocolic artery, and jejunoileal branches which are small and irregular. Findings are suggestive for mesenteric ischemia.

**Discussion:** Sclerosing mesenteritis is a rare disorder that affects the small bowel mesentery of predominately middle aged men. Symptoms include abdominal pain, bloating, distention, diarrhea and weight loss. The presentation is usually a manifestation of an impinging mesenteric mass resulting in symptoms of bowel obstruction. The pathophysiology remains largely unknown. Currently, there is no optimal treatment strategy. Consequently,

treatments have ranged from conservative management in asymptomatic patients, medical therapy, and surgical intervention in non-responders.

Sclerosing mesenteritis is frequently a relatively benign condition, although it can be a debilitating disease. Symptoms are usually a result of bowel obstruction; however patients may infrequently develop mesenteric ischemia as a result of mechanical compression of the abdominal vasculature. In this case, angiography suggests that our patient has developed compromised arterial blood flow leading to symptoms of ischemia. Our patient was initiated on Azathioprine four weeks earlier and levels of the metabolite 6-Thioguanine (6-TG) were being monitored. This case illustrates that alternative therapy, which includes revascularization or tailored medical therapy may be needed to prevent further complications in patients with sclerosing mesenteritis resulting in mesenteric ischemia.

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#### Evaluation of an Inpatient with Obscure Gastrointestinal Bleeding in the Community Hospital Setting

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The evaluation of obscure gastrointestinal bleeding has been revolutionized by the use of Capsule Endoscopy (CE). Studies have consistently shown the superiority of the capsule over small bowel series and traditional push enteroscopy. Though widely available, it is not however available in all locations. Older but more widely available studies for obscure gastrointestinal bleeding still have value.

A 67 year old male presented to a community hospital emergency room with syncope, lethargy, and shortness of breath with exertion. The patient reported one day of dark stools. He had no abdominal pain and denied the use of aspirin, NSAIDs, clopidogrel, or warfarin. Initial lab work showed a hemoglobin of 4.8 g/dl and an mcv of 64. Abdominal exam was benign. Rectal exam confirmed melena. The patient was admitted to a monitored unit and resuscitated with IV fluids and transfusion of packed red blood cells. Inpatient EGD the next morning was unremarkable. Colonoscopy after polyethylene glycol preparation showed black stool and dark clot in all colonic segments. During cecal washing, blood clot was observed passing through the ileocecal valve.

Once stabilized, since CE was not available in the hospital, the patient was discharged without further study. Outpatient CE performed seven days following initial presentation revealed an erythematous small bowel mass one hour into the recording. CT scan two days later identified a 5 cm mass in the abdomen. Surgical pathology of a proximal jejunal mass was consistent with a GIST. Post operatively the patient did well. Six month follow up blood counts were normal.

Though the weight of clinical evidence heavily favors CE as the most sensitive test for small bowel bleeding, clearly each case exhibits its own special considerations. While capsule endoscopy availability has expanded in the community, most CE units are outside the hospital, and therefore most studies are performed in an office based setting. For our patient, given the size and location of the lesion, it is very likely that further inpatient workup such as push enteroscopy or small bowel series would have made the diagnosis. While this patient's good outcome was not compromised by the diagnostic delay, this may not be the case for others. Our eagerness to provide the best and most up to date testing for our patients should not make us overlook the other valuable diagnostic tools at our disposal.

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#### False Negative Test for Gastroparesis from Technetium (Tc) Oatmeal Radionuclide Gastric Emptying (GE) Study; Lack of Standardized Updated Protocols for Tc GE in Community Hospitals

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We present a case of a strikingly false negative TcGE study, using oatmeal, a semi-solid, in a patient with significant gastroparesis, as well as results of an initial small survey of radionuclide TcGE protocols in local hospitals most of which were outdated, and did not conform to more recent standardized data.

A 42 yo man was referred for a second opinion for refractory dyspepsia and GERD. He had a 2–3 yr history of chronic recurrent nausea, episodic vomiting and erosive esophagitis which had responded poorly to bid PPI's, H2 blockers, and metoclopramide. Bravo pH testing had shown significant residual GERD on PPI therapy. A Tc oatmeal GE study off metoclopramide, done at the referring hospital, was interpreted as normal (T 1/2 31 min). Physical exam showed a succussion splash. The GE study repeated at a our tertiary referral hospital with standard 2 hour Tc egg sandwich technique showed severe gastroparesis (T 1/2 > 180 min). Patient was started on domperidone 10 mg qid, and lansoprazole solu-tabs 30 mg twice daily with marked improvement.

The Tc GE technique is the most widely used test for gastroparesis. Substrate type greatly affects the rate of emptying. Most published normal values for GE use a solid Tc egg substrate. Semi-solid oatmeal mixed with Tc has been used in pts who are allergic to eggs, with scant normal data, and no comparative data with standard egg sandwich technique. Yet oatmeal is the only substrate used for GE studies at the large hosp chain which referred our patient. A multi-center study published in 2001, has provided simplified reproducible 2&4 hr Tc egg GE methodology, requires few measurements and is reproducible. We initially polled 10 other hospitals, in the area and found none that followed recent published standard methodology, with wide variation. We found that patients with gastroparesis respond at times poorly to conventional PPI's. A solu-tab type PPI preparation significantly improves the GERD response. 1) Oatmeal is a poorly studied semi-solid substrate for Tc based gastric emptying study, and should be used only in true egg allergic patients. 2) The effect of gastroparesis on PPI bioavailability, should be further investigated.

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#### **An Unusual Case of Severe Pill Esophagitis Mimicking Herpetic Esophagitis, Caused by a New OTC NSAID – Containing Sleeping Aid**

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We present a case of severe NSAID induced esophagitis, mimicking severe herpetic esophagitis, caused by a new sleeping aid OTC preparation that combines naproxen and diphenhydramine. This type of preparation caused severe injury to the esophagus, its use as a bedtime sleeping aid, greatly increasing the risk of pill induced esophagitis. We could find no product labeling warning patients of this potential complication.

This 37 yo man with a hx of dyspepsia, IBS, and chronic insomnia, developed acute severe odynophagia, which did not respond to PPI's, or antacids, only able to swallow small amounts of liquids. He repeatedly denied taking any pills associated with pill induced esophagitis. Urgent EGD revealed very severe discontinuous ulcerations with almost complete slough of the distal esophageal mucosa, suggestive of severe herpetic esophagitis. Biopsies and viral cultures were negative for herpes. Patient improved with the addition of liquid sucralfate qid. On subsequent questioning he remembered taking a naproxen containing sleeping aid (Advil-PM®) at bedtime with little water for several days prior to the symptoms. The preparation was stopped, symptoms resolved, and repeat endoscopy showed healing of the ulcerated esophageal mucosa.

Many patients take sleeping aids for insomnia, that typically have acetaminophen and diphenhydramine, such as Tylenol PM®. We were surprised to learn of the existence of a similar OTC NSAID preparation (Advil PM®). In our previous case-controlled study (Gastrointest Endoscopy 2004;

59:AB240) NSAID's were the most common cause of pill induced esophagitis. A preparation that combines an NSAID with a sleeping aid, carries particular risk for inducing pill-induced esophagitis, due to its bed-time use. Patients need to be cautioned about this potential side effect of this type of preparation. The injury was particularly severe, but responded to NSAID cessation, and PPI and sucralfate therapy.

Clinicians need to be aware of new sleeping aid OTC preparations that contain NSAID's, caution patients about their potential for inducing pill esophagitis, and question patients with unexplained esophageal ulcerations and odynophagia about their use.

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#### **Asymptomatic Meckel's Diverticulum with Multi-Tissue Heterotopia**

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Meckel's Diverticulum (MD) is a congenital intestinal blind pouch resulting from an incomplete obliteration of the omphalomesenteric duct during the fifth week of gestation. It is present in 2% of the population with a male:female ratio of 3:1. Patients may be asymptomatic, with MD being identified intraoperatively, or symptomatically, with MD causing obstruction, intussusception, volvulus, bleeding & diverticulitis. We present a case of MD with unusual form of heterotopic tissue found incidentally.

Review of literature using Medline.

A 76 year old female was admitted for nausea, vomiting, crampy abdominal pain & constipation for a day. Her past history was significant for abdominal hernia with mesh repair 5 years prior. A CT Scan of the abdomen revealed multiple air-fluid levels suggestive of small bowel obstruction. She underwent abdominal exploration with adhesiolysis. A 3 cm × 2.5 cm × 2 cm normal looking MD was incidentally identified & was resected. Histopathological examination showed gastric heterotopia, exocrine & endocrine components of the pancreas. Pancreatic endocrine component was confirmed with immunoperoxidase stains namely, pancytokeratin, synaptophysin & chromogranin. The incidence of ectopic mucosa in MD varies from 15% to 50%. Ectopic gastric tissue is found in 60% to 82%, pancreatic in 1% to 16% & both in 5% to 12% of the cases. Meckel's scan is 80% sensitive in identifying MD, with sensitivity increasing with intravenous pentagastrin administration. Ectopic gastric mucosa is the commonest ectopic tissue in MD leading to hemorrhage and diverticulitis, whereas pancreatic tissue predisposes to bowel obstruction due to mass effect & leads to intussusception & volvulus. Surgery is recommended for incidental MD found during laparotomy in patients younger than 80 years. In our case, intestinal obstruction was caused by adhesions secondary to the previous hernia surgery & not due to MD.

Although, asymptomatic MD is of pathological interest for the complexity of tissue heterotopia which is involved, physicians should be aware of this entity because of its varied clinical manifestations when symptomatic.

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#### **Insulin and Dextrose in the Treatment of Hypertriglyceridemia Induced Pancreatitis (HIP)**

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Hypertriglyceridemia is thought to be the etiology in 3% of patients with acute pancreatitis, often associated with poorly controlled diabetes mellitus or chronic alcohol abuse. We present a case of HIP, treated using insulin & dextrose.

Review of literature using Medline.

We report a case of a 36 year-old male who presented with severe diffuse abdominal pain, nausea, vomiting & flexed contracture of his upper extremities. Patient did not have any past medical history or prescribed home medications. He had consumed moderate amounts of alcohol in the past with an episode of binge drinking prior to admission. Relevant physical findings included tachycardia, scleral icterus, epigastric tenderness & upper extremity tetany. White blood cell count was 9300/uL with 29% bands. Chemistries were significant for corrected calcium of 5.9 mg/dl & an anion gap metabolic acidosis with bicarbonate of 15 mM/L. Liver function tests revealed total bilirubin 3.1 mg/dl, AST 339 U/L, ALT 140 U/L & alkaline phosphatase of 253 U/L. Amylase was 256 U/L & lipase could not be assayed because the specimen was grossly lipemic. Abdominal ultrasound showed biliary sludge with no cholelithiasis. Computed tomography of the abdomen revealed peripancreatic fat stranding. Lipid profile showed triglycerides of 6850 mg/dl. Patient's pancreatitis was attributed to his hypertriglyceridemia. He was treated with intravenous fluids, prophylactic antibiotics, pain control & bowel rest. Calcium chloride infusion corrected the hypocalcemia & tetany. A novel therapy was employed to reduce triglyceride levels by starting an insulin & dextrose infusion. Insulin drip was started at 4 U/hour along with 100 ml of 10% dextrose infusion. Triglyceride levels decreased dramatically from the initial value to 1920 mg/dl the next day and 159 mg/dl on day 4 with resolution of pancreatitis.

Insulin is known to stimulate lipoprotein lipase activity and accelerate chylomicron degeneration thereby reducing serum triglycerides. This was the rational for insulin use in this case. The patient's response to this treatment is consistent with a few other rare reports in the literature which suggests that insulin/glucose infusions should be further evaluated in cases of HIP.

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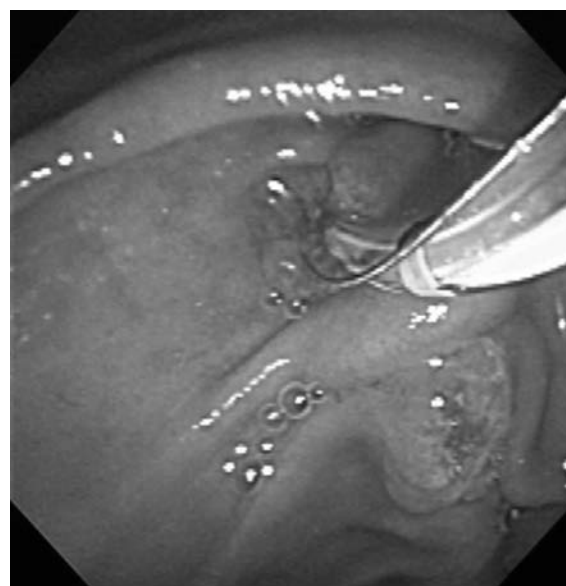
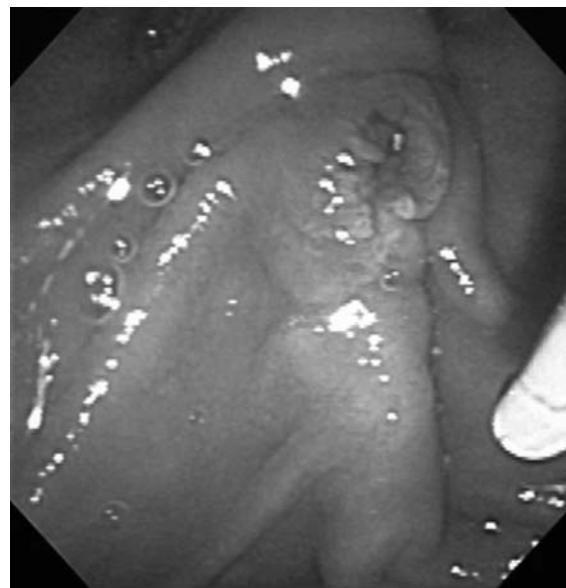
#### Rare Anatomic Variation of Ampulla of Vater

Patricia Laurel, Rahat Hussain, Muhammed G. Nathani\*. *Internal Medicine, UTHSCSA, Regional Academic Health Center, Harlingen, TX.*

**Introduction:** Ampulla of Vater refers to a confluence of distal common bile duct and main pancreatic duct in second portion of duodenum. In 10–15% of patients, the pancreatic duct and common bile ducts have separate openings into the duodenum. However, in most cases, the openings are within the same papilla (ampulla). We report a very unusual anatomic variation of Ampulla of Vater with evidence of duplication of ampulla. The pancreatic duct opening was in the the main ampulla and the common bile duct had a completely separate opening within a smaller ampulla about 2 cm proximal to the main papilla.

**Case Report:** A 29 year Hispanic female presented with a 3–4 month history of recurrent abdominal pain with occasional fever and chills. Physical examination was unremarkable. Laboratory data was within normal limits. Abdominal ultrasound suggested dilated common bile duct and cholelithiasis, with suspicion of choledocholithiasis. An ERCP was performed. The ampulla was identified but only pancreatic duct could be cannulated. Further careful exploration revealed another ampulla like structure 2 cm proximal to the main ampulla. This was cannulated and led to a dilated common bile duct with multiple filling defects. A relatively small sphincterotomy was performed because of smaller size of the ampulla and stones were extracted.

**Discussion:** This case presents a rare anatomic variation. Although she had recurrent biliary colic and ERCP confirmed choledocholithiasis, she did not develop pancreatitis. Choledocholithiasis is the most common cause of pancreatitis. However, our patient was protected from developing pancreatitis due to the separate opening of the common bile duct. If not correctly identified, this patient may have had serious complications from an access (precut) sphincterotomy of the main papilla, including severe pancreatitis and possible perforation.[figure1][figure2]



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#### Long Biliary Stent Causing Sigmoid Colon Perforation

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Distal biliary stent migration occurs in 5–10% of the cases; usually, the stent passes spontaneously through the rectum. Cholangitis, perforation, obstruction, and fistula formation are the reported complications. In our patient, biliary stent migration resulted in sigmoid colon perforation. We describe the clinical presentation, associated risk factors for colon perforation and review the published literature.

**Case report:** 70-Year-old male with Hepatitis C, Childs class A cirrhosis and unresectable hepatocellular carcinoma was referred for ERCP and stenting of segmental biliary obstruction caused by the tumor. Radio frequency ablation (RFA) was planned later in the week, but it was thought that the segmental biliary obstruction should be drained to prevent cholangitis after RFA. He has past history of open cholecystectomy 38 years ago, sigmoid diverticulosis and left inguinal hernia repair. Patient underwent ERCP and stent placement across the area of obstruction in the left intrahepatic ductal system. A10-Fr and 15 cm plastic biliary stent with a single external

flap and single internal flap was inserted uneventfully. 2 days after the stent placement, patient underwent RFA. 10 days later patient presented to the ER with worsening abdomen pain for 6 days and with signs of peritonitis. CT scan revealed free air in the abdomen, sigmoid diverticulae and a migrated stent in the abdomen outside the lumen of the sigmoid colon. Patient underwent laparotomy, which revealed ascites with fecal staining, a sigmoid resection with colostomy and peritoneal toilet was performed. The stent was found to be floating freely in the peritoneum and was removed. The patient's postoperative course was complicated by hypotension, respiratory failure, renal failure, and sepsis. Despite aggressive therapy he did not improve and was made comfort measures. Patient died on post operative day 8.

**Conclusion:** Although rare, intestinal perforation should be considered in patients presenting with acute abdomen and radiology findings confirming stent migration. In our review of literature, most of colon perforations occurred between 1–3 weeks after the biliary stent placement. Straight stents, papillary stenosis, adhesions, diverticular disease, colonic strictures and hernias were associated conditions. Our case illustrates the point that long (> 7 cm) straight biliary stents may not spontaneously pass with feces should they become dislodged and double pigtail biliary stents should be considered to minimize the risk of perforation.

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#### TB or Not TB: An Atypical Etiology of Colitis

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Bloody diarrhea is a common presentation in clinical practice. In the US, inflammatory bowel disease, ischemic colitis, and bacterial infections are most commonly responsible for these findings. Our aim is to present a case of colitis with bloody diarrhea with a rare etiology amongst long-term inhabitants of the United States.

A 42 year-old Haitian woman with a past medical history of cadaveric renal transplant secondary to glomerulonephritis was referred for consultation with complaints of bloody diarrhea, fevers, and chills. Eight months prior, she presented to an outside institution with similar complaints. Workup at that time yielded a diagnosis of Crohns colitis and the patient was started on oral mesalamine and a prednisone taper. Her symptoms never resolved. She was hospitalized at our institution with right upper lobe pneumonia for which she was started on broad-spectrum antibiotics. She denied abdominal pain or anorexia. Physical examination revealed a temperature of 101.3 Fahrenheit, right basilar crackles, and mild right-sided abdominal tenderness without rebound. CT scan of the abdomen demonstrated a 4 × 2 cm fluid collection without air-fluid levels adjacent to the transplanted kidney and thickening of the terminal ileum and cecum. Repeat colonoscopy showed right-sided ulcerations with the most prominent ulceration at the ileocecal valve. Biopsies showed acute colitis with lymphocytic infiltrates and no granulomas. Special stains for CMV, flow cytometry for lymphoma, and fungus were all negative. Stool studies were positive for acid-fast bacilli. Review of biopsies from the cecal ulceration showed AFB positivity as did sputum from the bronchoscopy. Subsequent PCR studies confirmed Mycobacterium tuberculosis in the sputum.

This case highlights several important points. In an immunocompromised patient with bloody diarrhea, atypical causes should be entertained. Similarities in the clinical presentation between Crohns colitis, CMV colitis, and TB colitis make a definitive diagnosis difficult, as they may mimic each other. With the burgeoning increase in immunocompromised patients as well as the advent of biologic therapies for IBD, there has been a marked resurgence in mycobacterial disease. Mycobacterial tuberculosis should be considered in these patients presenting with bloody diarrhea.

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#### EUS with Trucut Biopsy for Diagnosis of Intra-Abdominal Tuberculosis

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An 80-year Italian old male presented with left upper quadrant pain, excessive fatigue, weight loss and normocytic anemia. EGD revealed thickened and inflamed gastric mucosa and 2 submucosal gastric impressions. CT scan of the abdomen showed low attenuation lesions in the omentum adjacent to the stomach and low attenuation gastrohepatic ligament lymph nodes.

The working diagnosis was lymphoma. Using linear EUS and fine needle aspiration, tissue was collected for cytology and microbiology. Cytology was initially non-diagnostic, so Trucut needle biopsy was performed. Perigastric lymph nodes cytology was positive for necrotic material with numerous lymphoid cells. AFB and fungal studies were negative.

Trucut biopsy on pathology revealed necrotizing granuloma without acid-fast bacilli. 4 weeks later AFB culture grew M. Tuberculosis complex.

Another patient who was a 44-year-old male with AIDS presented with fever, dysphagia, vomiting, weight loss and intermittent non-bloody diarrhea.

On admission he was febrile and tachycardic. Physical exam revealed cachectic ill-appearing male. Abdominal examination was unremarkable. There was no palpable lymphadenopathy. Patient was anemic; CD4 cell count was 5.

EGD revealed extrinsic compression of the stomach. CT scan of the abdomen showed a mass in the splenic hilum, indenting the posterior aspect of the stomach, and smaller masses in the paragastric region. EUS was performed with multiple fine needle aspirations of the lesions and but it did not provide definitive diagnosis, so EUS was repeated with Trucut biopsy.

Histology revealed necrotic tissue mixed with lymphoid cells, histiocytes, caseating granuloma with presence of AFB, further identified as Mycobacteria tuberculosis. Patient was treated with four-drug regimen; his condition improved and he was discharged.

Diagnosis of abdominal tuberculosis presents a challenge because it is uncommon, inaccessible, and yields few numbers of bacilli on FNA.

It is important to realize, that TB seems to be resurging and abdominal TB needs to be considered in the differential in both immunocompromised and immunocompetent patients.

In the above 2 cases we show that EUS with Trucut needle tissue acquisition can be an accurate and safe method of diagnosing lesions accessible through the gastrointestinal tract. EUS guided Trucut biopsy played crucial role in diagnosis of intra-abdominal tuberculosis in both the immunocompromised and immunocompetent patient.

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#### A Case of Fatal Polycystic Liver Disease

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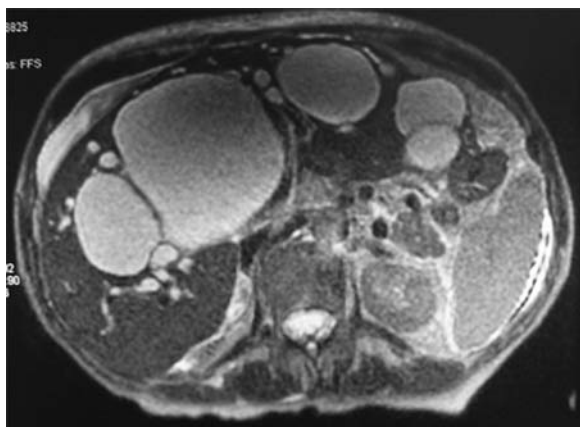
Autosomal dominant polycystic kidney disease (ADPKD) is the most common hereditary renal disease which affects 1/400 to 1/1000 live births. Liver involvement is the most common extra-renal manifestation. The prevalence and number of hepatic cysts in patients with ADPKD increase with age, female sex, severity of renal disease and use of exogenous female steroids. Polycystic liver disease (PLD) occurs alone as autosomal dominant polycystic liver disease (ADPLD) or in combination with ADPKD. Jaundice and hepatic failure are unusual features of PLD. Here we present a case of an advanced PLD.

A 79 yr old female with history of PLD, ADPKD presented with fatigue, anorexia, abdominal pain and distension, ten pounds weight loss, dark urine and itching. No history of alcohol, hepatotoxic drugs, tattoos or viral hepatitis. Examination showed icteric sclerae and mucous membranes, distended abdomen with fluid wave, hepatomegaly and pedal edema.

Pertinent laboratory results included hb 10.1 g/dl, hct 31%, plt 279 k/cumm, BUN 22 mg/dl, creatinine 0.7 mg/dl, alk phos 366 IU/L, AST 53 IU/L, ALT 22 IU/L, total bilirubin 9.1 mg/dl, direct bilirubin 5.5 mg/dl, indirect bilirubin 3.6 mg/dl, PT 16.6 sec, INR 1.4, albumin 1.5 g/dl. CAT scan of abdomen showed multiple hepatic cysts with compression of surrounding parenchyma and bilateral renal cysts. MRCP revealed compression of extra

hepatic biliary ducts by a large left lobe cyst. As the patient was not a candidate for transplant, a cholecystectomy and choledochoduodenostomy were done to alleviate the distal obstruction. Post-operatively the patient succumbed to overwhelming sepsis and encephalopathy.

While most patients with PLD are asymptomatic, some patients may experience abdominal pain, early satiety, and shortness of breath due to massive liver enlargement. Rarely patients such as ours can have ascites, hepatic failure and encephalopathy. Treatment of symptomatic liver cysts is comprised of somatostatin analogues, aspiration, sclerotherapy, unroofing, internal drainage with cystojejunostomy or fenestration. In extreme cases hepatic resection or liver transplantation are options.[figure1]



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### The Misplaced Shoe Polish Bottle!

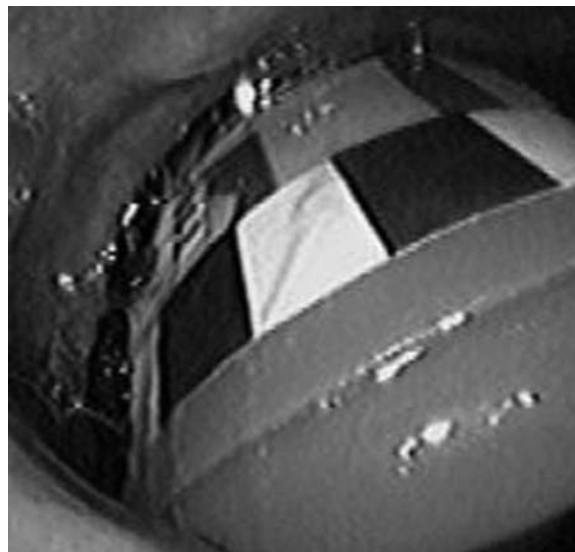
Rohit Jindal, MD, Edmond Bouassaf, MD, Ayse Aytaman, MD\*. Gastroenterology, VA NYHHS, Brooklyn, NY and Gastroenterology, SUNY Downstate Medical Center, Brooklyn, NY.

Rectal foreign bodies of various shapes and sizes have been reported. Such patients usually present with pain and obstructive symptoms however presentation is often delayed due to embarrassment. Morbidity is due to bleeding, laceration or perforation and is usually complicated with multiple attempts at self removal. We present the case of a patient with a considerably large foreign body impacted proximal to the rectosigmoid junction which was successfully removed by endoscopy.

**Case Presentation:** A 43 y man presented with rectal pain and mild rectal bleeding for two days. He admitted to using objects for rectal insertion two days prior to presentation. The patient had made several unsuccessful attempts to evacuate the rectum using digital manipulation and laxatives. On rectal exam, the smooth edge of a foreign body was palpable. Abdominal xray was suggestive of a metallic spring device in the sigmoid. Sigmoidoscopy revealed the base of a large plastic bottle at 5 cm from the dentate line [Fig. 1]. The scope was carefully advanced along the side of the bottle and its proximal end was noted to be at 30 cm. Attempts to grab the bottle with forceps of various sizes were unsuccessful. It was also not possible to snare the bottle as its diameter was larger than the largest available endoscopic snare. Finally, 9.5 in Foerster forceps with serrated jaws were inserted carefully alongside the scope and under visual guidance, the base of bottle was grasped. The forceps were slowly pulled out as the patient bore down. The object turned out to be a plastic liquid shoe polish bottle 20 cm long and 4.5 cm in diameter. A check sigmoidoscopy revealed minimal mucosal trauma at the rectosigmoid junction but no perforation. Repeat abdominal xray was normal and the patient discharged after observation for a few hours. Review of literature revealed this to be a unique case of a liquid shoe polish bottle recovered from the rectum using endoscopy.

**Discussion:** Transanal removal of large objects impacted above the rectosigmoid junction is difficult. However, endoscopic removal should be preferred

and attempted prior to open surgical approach as it is safe, less morbid and cost effective.[figure1]



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### DIC as a Complication of HHT or Osler-Weber-Rendu Syndrome

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The possibility of disseminated intravascular coagulopathy (DIC) as a complication of hereditary hemorrhagic telangiectasia (HHT) has been described in the past[1]. However, due to the low incidence of HHT, information on the topic is scarce. We present a case of HHT complicated by DIC to support the clinical awareness needed with regards to DIC resulting in bleeding as a presentation of HHT.

A 72 year old female presented with a severe episode of epistaxis and was found to be in DIC. She had been suffering from recurrent episodes of epistaxis for over 5 years. Her past medical history included pulmonary embolus, COPD, hypertension and diverticulosis. Her family history included recurrent epistaxis in her father and son. Physical examination on presentation demonstrated a telangiectetic lesion on the tongue and fingertips and dried blood in her right nares. Laboratory data revealed WBC 7.67, HCT 37, MCV 86.2, Platelets 114, PT 24, INR 2.1, Fibrinogen <70, and DDimer >5250. BUN 8, Cr 0.8.

Endoscopy performed for hematemesis confirmed gastric arterio-venous malformations (AVMs). CT angio of abdomen and chest demonstrated pulmonary, liver, and gastrointestinal tract AVMs. Small bowel capsule study confirmed gastric AVMs with no small bowel AVMs. Genetic testing demonstrates single nucleotide (A) deletion at position 364 of the ALK-1 gene causing a truncated ALK-1 protein.

A clinical diagnosis of HHT was confirmed.

This case adds to the literature in support of the clinical relevance of DIC as a complication of HHT. Furthermore, in this case it was a part of the acute presentation which led to the diagnosis of HHT. [1] Ann N Y Acad Sci, 1981;370:851-4

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### Primary Duodenal Mucosa-Associated Lymphoid Tissue Lymphoma Treated with Rituximab

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MALT lymphoma is the most common primary lymphoma of the GI tract. Though gastric MALT lymphoma is well described, only 17 cases of primary duodenal MALT lymphoma are reported. The use of rituximab has never been reported.

A 64 year old man with hypertension had three years of intermittent GI bleeding. Multiple endoscopies showed duodenitis with ulceration. Biopsies of the stomach and duodenum on five occasions showed peptic duodenitis without *H. pylori*. Work-up for Zollinger-Ellison syndrome was negative and all NSAIDs were discontinued without improvement. Despite a highly selective vagotomy, the duodenitis and ulcerations persisted, prompting referral.

On presentation, the patient was taking esomeprazole twice daily and ranitidine nightly. Four weeks after an empiric course of *H. pylori* therapy, endoscopy showed duodenal erosions with biopsies revealing duodenitis. Sucralfate was started and endoscopy three months later showed duodenitis with an eosinophilic infiltrate. Cromolyn was prescribed and endoscopy four months later was unchanged. However, biopsies revealed a dense CD20-positive lymphocyte infiltrate. MALT lymphoma was confirmed by flow cytometry. PET scan showed increased radiotracer uptake in the duodenum with no metastases. The patient did not want extensive chemotherapy, radiation therapy, or surgery; therefore, a one month course of rituximab was given. A follow-up PET scan showed persistent, though notably less, uptake in the duodenum. An endoscopy revealed persistent MALT lymphoma. In the setting of only a partial response to rituximab, the patient underwent radiation therapy.

Of the reported cases of primary duodenal MALT lymphoma, only three patients responded solely to *H. pylori* eradication. All other cases were treated with either chemotherapy or surgery. Different chemotherapeutic regimens include oral cyclophosphamide; CHOP followed by vinblastine/etoposide/epirubicin/prednisone; CVP; and clarithromycin monotherapy. In the remainder of cases, surgery was the preferred. We avoided more toxic regimens for rituximab, a chimeric monoclonal antibody to CD20-positive lymphocytes. Rituximab has demonstrated efficacy in a variety of lymphomas and with response rates as high as 64% in gastric MALT lymphoma. There are no reports of its use in primary duodenal MALT lymphoma. Given rituximab's ease of administration and reasonable side effect profile, it may be a viable alternative for treatment in the absence of response to *H. pylori* eradication.

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### Fatal Small Bowel and Colonic Ischemia after Sodium Phosphate Bowel Preparation

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A 69 year old woman with a history of breast cancer, COPD, osteoporosis, and hypertension was scheduled for a colonoscopy for heme positive stools and constipation. Serum creatinine, electrolytes, and hepatic enzymes were normal, and she was instructed to use a sodium phosphate (NaP) bowel preparation. On the day prior to her procedure she ingested 45 ml of an oral NaP solution, and subsequently developed nausea, vomiting and abdominal pain. Upon presentation, she was slightly tachycardic but her blood pressure was normal. Her abdomen was moderately distended with decreased bowel sounds. Serum sodium was 136 mEq/L, potassium 3.6 mEq/L, chloride 96 mEq/L, bicarbonate 16 mEq/L, blood urea nitrogen 12 mg/dL, creatinine 1.3 md/dL, lactate 1.7 mmol/L, phosphate 13.6 mg/dL, and calcium 9.9 md/dL. Computed tomography of the abdomen showed marked feces in the colon with no free air or obstruction. Nasogastric and rectal tubes were placed, and non-phosphate based laxatives administered, without improvement in her abdominal pain. Thirty-six hours later she developed cardiopulmonary distress and was transferred to the intensive care unit. Flexible sigmoidoscopy showed dusky mucosa and she was taken emergently to the operating room. The entire colon and a small portion of the terminal ileum appeared non-

viable, and a total colectomy with ileostomy was performed. The following day her lactate had risen to 4.3 mmol/L, the ileostomy appeared necrotic and she was taken back to the operating room for a revision with resection of approximately fifteen centimeters of ischemic ileum. The pathology was consistent with diffuse ischemia and mucosal necrosis. Her hospital course was complicated by nosocomial infection, pneumonia with bilateral effusions, poor wound healing, refractory hypotension, and inability to wean from the ventilator. Her family decided to withdraw support and the patient died. There have been multiple cases of acute phosphate nephropathy resulting from NaP use that led to an FDA warning in 2006. However, in this case despite the hyperphosphatemia the patient never developed significant renal failure. In fact, her phosphorus levels and creatinine normalized and her urine output remained adequate. Fatal small bowel and colonic ischemia related to the use of a NaP bowel preparation has not been reported in the absence of renal failure.

## 676

### Strongyloidiasis Manifesting as Colonic Polyps Successfully Treated with Ivermectin

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A 75 year old male well compensated cirrhotic presented for surveillance colonoscopy three years after undergoing a left hemicolectomy for a large villous adenoma with HGD. Patient also with History of prostatic Ca treated with RT. He has had intermittent diarrhea over several years. He was found to have peripheral eosinophilia of 39%.

Colonoscopy revealed 20–30 polyps, scattered throughout the colon, ranging in size between 3 mm and 1 cm. Eight of these polyps were either biopsied or removed endoscopically. Pathology from all samples showed inflammatory polyps with marked eosinophilia, eosinophilic cryptitis and cryptal abscesses. Exam of stools showed few *Strongyloides Stercoralis* larvae. Accordingly, the patient was treated with two doses of Ivermectin at 24 hours interval.

At eight-week follow up, there was resolution of the diarrhea and hematochezia. CBC showed improvement of the peripheral eosinophil count to 7% of CBC. Colonoscopy revealed one 3 mm polyp, which, on biopsy showed no eosinophilia. Random colonic biopsies showed mild chronic inflammation with no eosinophilia.

**Conclusion:** *Strongyloides* infection should be considered in patients with a history of chronic diarrhea and multiple polyps on endoscopy. A history of



travel to an endemic area is suggestive. Two consecutive doses of Ivermectin can be considered as an effective treatment regimen.[figure1]

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### **Certolizumab Pegol Treatment of Crohn's Disease in a Patient Who Had an Adverse Reaction to Infliximab: A Case Report**

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**Patient history:** A 34-year-old male patient (weight 69 kg; height 179 cm) was admitted to hospital in October 2004 with severe abdominal pain and diarrhea. At admission, he had a Crohn's Disease Activity Index (CDAI) score of 243 points and reported more than five loose bowel movements per day (often with blood). Endoscopic examination and CT scans revealed moderate to severe lesions in the terminal ileum and colon ascendens, but there were no fistulae or stenoses.

**Initial therapy:** Treatment with azathioprine and oral cortisone for 5 months failed to achieve a satisfactory response (2–3 intense, loose bowel movements/day, with spasms and blood; CDAI score of 209 points).

**Infliximab therapy:** Therapy with infliximab (300 mg iv infusion at 0, 2, and 8 weeks, and then every 8 weeks) was initiated in February 2006. After the third infliximab infusion, the patient developed signs of severe acute pancreatitis and hypotension, accompanied by massive diffuse abdominal pain, fever, and vomiting. The patient was hospitalized and examinations indicated serious pancreatitis with swelling in the pancreatic head, ileum terminalis, and colon ascendens. Antibodies against infliximab were not measured. Following treatment with analgesics, parenteral nutrition, and metronidazole, the patient's condition stabilized and he was subsequently discharged. Although 5% of infliximab infusions are associated with nonspecific adverse reactions, severe acute reactions such as acute pancreatitis are rare.

**Therapy with certolizumab pegol:** After discharge from hospital, the patient's clinical condition soon worsened (severe diffuse abdominal pain, 5–7 loose bowel movements/day, with blood; CDAI score of 214 points). The patient began treatment with certolizumab pegol (induction with 400 mg subcutaneously at Weeks 0, 2, and 4, and then 400 mg every 4 weeks). The patient's condition improved after the second certolizumab pegol injection (2–3 loose bowel movements/day, very few pain episodes, and CDAI score of 134 points). After 6 months' certolizumab pegol therapy, the patient showed significant improvement (almost no diarrhea, only occasional pain, some weight gain, and CDAI score of 92 points).

Certolizumab pegol provided effective treatment of Crohn's disease for this patient who had previously reacted badly to treatment with infliximab. This case illustrates that certolizumab pegol may offer a viable rescue therapy for a patient with Crohn's disease who experiences such a reaction to infliximab. Certolizumab pegol was provided by UCB.

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### **Delayed Life Threatening Rectal Bleeding after Trus-Guided Prostatic Biopsy**

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Rectal bleeding is one of the complications of TRUS-guided prostate biopsy, but is usually mild and stops spontaneously. We report a case of delayed severe rectal bleeding after TRUS-guided prostate biopsy that required emergency colonoscopy and clipping of the bleeding vessel.

A 56 year-old man presented with dysuria, fever and chills. Three days earlier he underwent TRUS-guided prostate biopsy which was uneventful. His medical history included hypertension and dyslipidemia. His temperature was 105.1, pulse was 144 and BP was 106/75. He also had distended urinary bladder and tender prostate. Blood tests showed a WBC count of 15.4, hemoglobin of 11.9, and platelet count of 253. Coagulation profile was normal. Urine analysis showed 269 WBC and 116 RBC per HPF. A Foley's catheter was inserted and he was treated with antibiotics. He improved over the next 3 days. However, on the fourth day, he passed a large bowel movement of bright blood and developed hypovolemic shock. While

being resuscitated emergent colonoscopy was done. Colonoscopy showed a large bleeding vessel at the biopsy site and the bleeding was successfully controlled using hemostatic clips. The patient was stabilized with 2 units of PRBC and had no further bleeding since then.

Mild hemorrhagic complications are common problem after transrectal prostate needle biopsy. Bleeding commonly occurs directly after the procedure and is usually controlled by applying pressure at the biopsy site. Only few cases of severe rectal bleeding which required invasive procedures were reported. We also found one case report of delayed rectal bleeding after 5 days. Our patient developed rectal bleeding 7 days after biopsy, which represents secondary hemorrhage due to urinary infection. Our literature review found no prior results of colonoscopic treatment of bleeding site with clipping of the blood vessel. We propose this useful procedure in similar cases.

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### **Bread Bag Clip Ingestion: A Rare Cause of Upper Gastrointestinal Bleed**

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An 83-year-old man with a history of macular degeneration and atrial fibrillation on coumadin was admitted to an outside hospital with hematemesis and profound anemia. EGD revealed a 1 cm clean-based cratered ulcer in the duodenal bulb. He was discharged off coumadin and presented to our institution two days later with an acute stroke. Prior to the reinstitution of anticoagulation, EGD was performed to evaluate the prior ulcer. A side-viewing endoscope was used for full visualization and showed a foreign body eroding into the posterior duodenal wall with an underlying deep ulceration. Endoscopic removal was not possible due to strict adherence to the duodenal mucosa. Exploratory laparotomy revealed a bread clip eroding into the duodenal wall in close proximity to a duodenal diverticulum. Duodenotomy and extraction of the clip was performed. The patient did not recall having ingested the bread clip.

Bread clips are rarely found as foreign bodies in the gastrointestinal tract. When present, the clip can adhere to the mucosa causing obstruction, perforation, or bleeding. There have been twenty three reported cases of bread clips found in the gastrointestinal tract. Bowel obstruction and perforation are the most common clinical presentations. Our patient is the second reported case world-wide of gastrointestinal bleeding caused by a bread clip. The small bowel is the most common site of impaction thought to be due to the smaller diameter and irregularly folded mucosa. Esophageal and colonic impactions have also been described. Complications may arise up to years after ingestion. As there was no expiration date on our patient's clip, it was impossible to estimate the time from ingestion. Most cases of ingested bread clips are elderly, edentulous patients. Our patient's accidental ingestion was due to his severe vision impairment. Diagnosis is often difficult secondary to unawareness of ingestion and radiolucency on x-ray. Therefore, impaction of a radiolucent foreign body should always be considered in the differential of gastrointestinal bleeding. Given the significant morbidity and mortality related to bread clip ingestion, some countries have eliminated their use while others are looking for a newly-designed clip.

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### **Mycobacterium Avium Complex Infection of the Duodenum**

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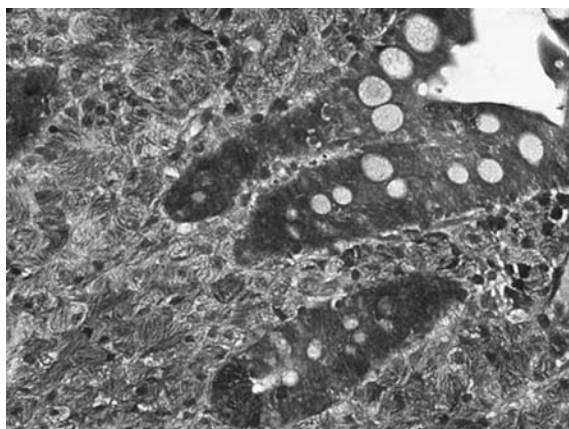
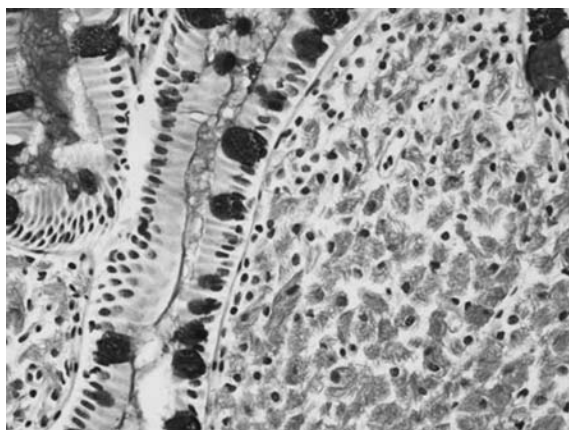
A 31-year-old woman with AIDS was admitted with abdominal pain, non-bloody diarrhea, and recurrent fever. She reported fatigue, weakness, and weight loss of 14 kg over six months. Laboratory testing revealed normo-



cytic anemia, minimally elevated transaminases and alkaline phosphatase, and hypoalbuminemia. The total bilirubin and LDH were normal. Upper endoscopy revealed a normal esophagus and stomach. The duodenal mucosa was granular and firm with tan-yellow nodules and plaques. Microscopic examination of biopsy specimens prepared with periodic acid-Schiff (PAS) and Fite's acid fast stains revealed abundant histiocytes within the lamina propria containing a dense array of filamentous inclusions. DNA probe of a positive acid-fast blood culture confirmed *Mycobacterium avium* complex (MAC) infection.

The prevalence of gross GI mucosal involvement in disseminated MAC has not been clearly defined and endoscopic findings are variable. In a review of 55 cases of disseminated MAC infection in patients with AIDS where endoscopic findings were reported, the most common finding was multiple raised nodules that were yellow, white, yellow-whitish, or pink in color in 38%. The mucosa was normal in 36%. Other non-specific findings such as erythema, edema, and ulcerations were encountered less frequently. The duodenum was involved in > three quarters of the cases described, while the rectum was involved in nearly 25%.

Histologic examination of biopsy specimens is essential when endoscopically evaluating patients with suspected disseminated MAC as similar clinical manifestations, endoscopic findings, and histologic findings are encountered in *Tropheryma whipplei* infection. In contrast to MAC, organisms in Whipple's disease are rounded and sickle-shaped, intracellular and extracellular, and resist acid fast staining. Whipple's disease is rarely reported in patients with AIDS.[figure1][figure2]

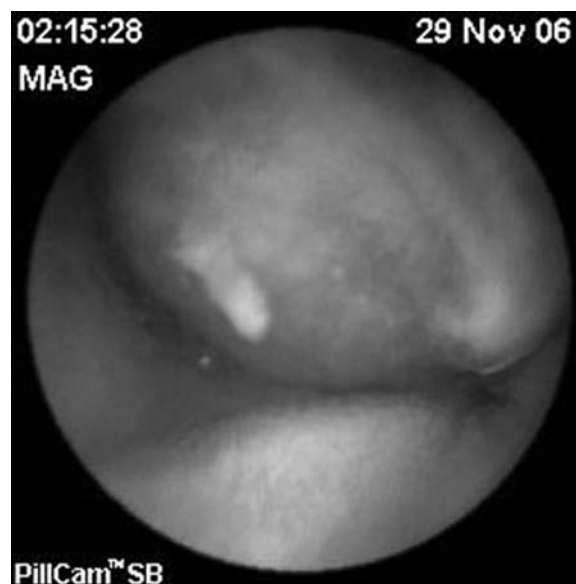


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To be familiar with the diagnosis, treatment, and prognostic factors for sarcomas in the GI tract.

**Case:** A 50 year old female was referred for evaluation of obscure GI bleeding presenting with melena and iron deficiency anemia. Past medical history revealed a diagnosis of soft tissue sarcoma involving the buttocks, with subsequent spread to her heart, colon, and adrenal gland. She completed multiple courses of chemo-radiation therapy and underwent a right hemicolectomy. At the time of referral, medical oncology felt that her disease was stable based on whole body CT scan imaging. Physical exam revealed pale conjunctiva and sacral changes consistent with a prior resection and radiation. Laboratory data confirmed anemia (Hgb 7.8 g/dL, Hct 25%, iron 10 mcg/dL). Upper GI endoscopy with small bowel enteroscopy to the proximal jejunum and colonoscopy failed to demonstrate any active GI bleeding source. Capsule endoscopy was performed and revealed 2 large, ulcerated submucosal lesions with active bleeding from the mid-jejunum to the distal ileum (Figure). Intraoperatively an area of intussusception with 2 intraluminal masses was located approximately 1 1/2 feet from the ileocolic anastomosis and was resected. Pathology confirmed metastatic high-grade sarcoma.

**Discussion:** Soft tissue sarcomas are rare malignant tumors, accounting for <1% of all new cancers/year. They arise from mesenchymal tissue with approximately 80% arising from soft tissue and 20% from bone. Besides metastatic spread to the small intestine, sarcomas can present as primary small bowel malignancies. In prior case series, clinical presentations of sarcomas of the small intestine (metastatic or primary) include an abdominal mass, pain, weight loss, GI hemorrhage, obstruction, intussusception, and perforation. The treatment of choice is surgical resection with intent to obtain adequate negative margins. The role of adjuvant chemotherapy remains controversial with studies showing varying results. With regards to prognosis of these tumors, histologic grade has borne out to be the most significant factor affecting survival.[figure1]



#### Metastatic Soft Tissue Sarcoma Detected by Small Bowel Video Capsule Endoscopy

Jennifer Weiss, MD, Sharon Weber, MD, Mark Reichelderfer, MD, Deepak Gopal, MD\*. Section of Gastroenterology & Hepatology & Dept. of

#### Four Different Presentations of a Rare Disease – Whipple's Disease

Bogdan Cristescu, MD, Safak Reka, MD\*. Digestive Diseases, SUNY Downstate Medical Center, Brooklyn, NY.

Whipple's disease (WD) is a rare chronic infectious multisystem disease caused by bacterium *Tropheryma whipplei*. Only about 1000 cases have



been reported to date. We describe our experience with 4 cases diagnosed with WD between 2002 and 2007: first 3 cases from Brooklyn, New York and case #4 from Western Massachusetts.

**Case #1:** A 72 year-old (yo) Caucasian male from Spain, living in Brooklyn since 1975, presented with 30 lbs weight loss, pulmonary nodules and retroperitoneal lymphadenopathy. Lymph node biopsy revealed foamy macrophages (FM) containing periodic acid-Schiff (PAS) positive (+) material and negative Ziehl-Neelsen stain (ZN). Retrospectively, he had arthralgia for 10 years and developed intermittent diarrhea, epigastric pain and progressive cognitive decline for the last 6 months. Laboratory data were significant for anemia and evidence of malabsorption. On upper endoscopy (EGD) duodenal mucosa had small lymphangiectasia and biopsy was consistent with WD with PAS + FM in lamina propria (LP).

**Case # 2:** A 61 yo Caucasian male from Russia, living in Brooklyn for the last 7 years, with long history of arthralgia was evaluated for iron deficiency anemia. Colonoscopy was unrevealing and EGD showed normal appearing duodenal mucosa with distended villi by FM PAS + and negative ZN on biopsies, consistent with WD.

**Case #3:** A 25 yo African American male presented with diarrhea for 1 year. Colonoscopy with ileoscopy revealed erythema of the terminal ileum mucosa with PAS + FM on biopsies. EGD confirmed the diagnosis of WD with similar findings on duodenal biopsy.

**Case #4:** A 41 yo Caucasian male of Irish descent, with history of seronegative polyarthritis on treatment with high doses of aspirin and intermittent steroids presented with an episode of diarrhea for 4 weeks with negative work-up including colonoscopy. The episode resolved, but subsequently the patient had recurrence of diarrhea and weight loss. On EGD duodenal mucosa appeared flat, pale and biopsies showed PAS + FM in LP suggestive of WD. The diagnosis was confirmed by a PCR assay.

All patients were treated with Ceftriaxone for 2 weeks followed by Trimethoprim-sulfamethoxazole for 1 year. Diarrhea and anemia resolved and arthralgia was significantly improved in all patients. Patient in case #1 had weight gain and improvement in adenopathy and cognitive function.

**Discussion:** WD has a variety of clinical manifestations and should be considered in patients who present with migratory arthralgias of the large joints, weight loss, diarrhea, and abdominal pain.

## 683

### Metastatic Lobular Breast Cancer to the Gastrointestinal Tract: An Unusual Case Report

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We report a rare case of lobular breast carcinoma metastatic to the stomach and colon. A 54-year-old patient had undergone left lumpectomy with axillary dissection and postoperative radiation therapy two years earlier. Currently, the patient presented with anemia (Hgb/Hct: 9.0 g/L/27.1%). Gastroscopy showed hiatal hernia while colonoscopy revealed nodular changes in the mucosa and diverticulosis. Biopsies from the gastric antrum and colon showed poorly differentiated carcinoma within the lamina propria with some of the tumor cells showing signet ring cell features. Histologically the carcinoma was similar to the invasive lobular breast carcinoma from two years ago. Immunohistochemical analysis revealed positive staining for CK7 and GCDPF-15 and few cells weakly positive for progesterone receptors, confirming breast origin of metastatic tumor. Staining for estrogen receptor marker and CK20 was negative. Nuclear Medicine bone scan showed no evidence of bone metastasis. The patient received aggressive systemic chemotherapy.

Breast carcinoma is the most common malignancy in women and metastatic breast cancer typically involves lymph nodes, lungs, bones, brain and liver. Gastrointestinal metastases is less common and usually derive from lobular

rather than ductal breast carcinoma, remain asymptomatic for a long time and present as a late event in the progression of the disease. Since lobular breast cancer has an unpredictable metastatic pattern such as hematogenous spread to distant organs prior to regional lymph node involvement, any specific or nonspecific symptoms in patients with known lobular breast carcinoma should cause a high suspicion of metastasis. Endoscopic exploration, adequate biopsies should be followed by histological and immunohistochemical analysis of gastric and colonic mucosal malignancies, further comparing with the histological features of original breast carcinoma. In summary, evaluation of any gastrointestinal symptoms in patients with history of invasive lobular breast carcinoma followed by pathologic and immunohistochemical analysis is essential in establishing an early diagnosis of metastatic lobular carcinoma and avoiding unnecessary surgical treatment.

## 684

### C difficile Enteritis in Ileostomy Patients: Report of Three Cases and Review of the Literature

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*C. difficile* (CD) is the most common cause of nosocomial infectious diarrhea and is generally considered a colonic pathogen. CD small bowel enteritis (CDSBE) has only rarely been reported. We describe the clinical course and treatment of 3 ileostomy patients with diarrhea due to CD.

**Case #1:** 48 YOM s/p colectomy and ileostomy for Crohn's disease 2 yrs previously presented with fever, nausea, vomiting, abdominal pain, increased ileostomy output, and marked dehydration. Antibiotics had been administered 3 months previously. Ileostomy CD toxin was positive by ELISA. He responded to a standard course oral metronidazole and vancomycin with resolution of symptoms and negative repeat CD toxin after treatment.

**Case #2:** 72 YOM s/p colectomy and ileostomy for ulcerative colitis 24 yrs earlier presented with a low-grade fever and non-bloody diarrhea of 1-month duration. There was no antecedent antibiotic use. Ileostomy CD toxin was positive by ELISA. He was initially treated with metronidazole, which was switched to oral vancomycin. He responded to 2 weeks of vancomycin, but relapsed following discontinuation and received a 1-month course of vancomycin with clearance of the toxin.

**Case #3:** 39 YOM with severe acute alcoholic pancreatitis required a total abdominal colectomy and ileostomy for colonic ischemia. He required multiple courses of antibiotics and subsequently developed a high ileostomy output. Ileostomy fluid CD toxin was positive and he responded to a standard course oral metronidazole and vancomycin.

**Discussion:** CDSBE has been reported in 20 patients in the literature, but only previously in ten ileostomy patients, most of whom were detected in the early post-operative period (<90 days). In only 3 cases in the literature was CDSBE diagnosed > 90 d following surgery in ileostomy patients. We report 2 more such cases, and a third in the early post-operative period. Most patients have a history of antibiotic use and present with increased ileostomy output. Most respond to standard therapies (oral metronidazole or oral vancomycin). Relapses may occur.

**Conclusion:** *C. Difficile* enteritis is a potential cause of high ileostomy output and should be in the differential diagnosis. Treatment with oral metronidazole or vancomycin is generally effective.

## 685

### An Undiagnosed Case of Cholecystitis and Salmonella Vertebral Osteomyelitis: From Gut to Bone

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A 66-year-old female was transferred to our institution complaining of a 3-month history of back pain, left leg numbness and weakness. She had initially been diagnosed with sciatica and received a steroid injection in her

left buttock. Her symptoms got progressively worse. During a local work-up, she had also been diagnosed with a urinary tract infection (UTI) and treated with a 7-day course of trimethoprim/sulfamethoxazole.

Magnetic resonance imaging (MRI) of the spine was then performed at her local facility and this showed a mass. The abnormal tissue was surgically excised but the pathology report commented on the absence of malignancy only. She continued to feel unwell and she was transferred to our institution, where a new MRI of the lumbar spine showed a probable infectious process in the L3 and L4 vertebral bodies with near-total collapse anteriorly.

New urine and blood cultures grew Gram negative bacilli. The same organism was grown from a lumbar spine biopsy. All cultures eventually grew nontyphoid *Salmonella*. It emerged that the diagnosis of UTI a month earlier had been based on a urine culture growing *Salmonella*. CT of the abdomen showed evidence of cholecystitis but no evidence of an abdominal aortic aneurysm.

The patient denied any gastrointestinal symptoms. She and her husband admitted to frequent ingestion of rare-cooked beef, though not poultry or eggs. She underwent cholecystectomy and a number of neurosurgical and orthopedic procedures. Gallbladder pathology revealed acute and chronic cholecystitis with focal abscess formation. She required a prolonged hospitalization and was discharged home on intravenous antibiotics.

*Salmonella* vertebral osteomyelitis (SVO) primarily involves the lumbar spine. The dominant features are fever and back pain. Diarrhea is uncommon in SVO, although gastroenteritis is the most common clinical syndrome associated with *salmonella* infection. *Salmonella* is frequently harbored in the gallbladder. Blood cultures are positive in 48% of the SVO cases. The condition requires long-term antibiotic management and some cases require surgery. Infected abdominal aortic aneurysms are associated with high mortality and need to be excluded in patients older than 50 years of age with *Salmonella* bacteremia or evidence of deep organ infection. The presence of *Salmonella* in the urine should not be treated as a UTI and should prompt immediate work-up for bacteremia and other tissue involvement.

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### Jejunal Ulcerations and Ascites as Presenting Manifestations of Henoch-Schonlein Purpura

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A 59-year-old man presented with a five day history of melena, hematemesis and progressive abdominal distention. There was no prior history of gastrointestinal bleeding. Physical exam was significant for mild abdominal tenderness with shifting dullness. Rectal exam revealed melena. CT scan of the abdomen and pelvis showed moderate ascites, patent mesenteric vessels, normal liver morphology, and segmental jejunal wall thickening with mild dilatation. Paracentesis revealed clear fluid with a serum-ascites albumin gradient of 0.9 consistent with a non-portal hypertensive etiology. Enteroscopy was significant for multiple cratered ulcers extending from the proximal to mid-jejunum with stigmata of recent bleeding. Biopsies of the jejunal lesions were consistent with mucosal ulceration. Intravenous steroids were initiated for a presumptive diagnosis of Crohn's disease. One week later, the patient developed acute renal failure and a purpuric rash involving the hands, bilateral lower extremities and buttocks. Skin biopsy showed a leukocytoclastic vasculitis. Immunofluorescence stain was positive for IgA. A diagnosis of Henoch-Schonlein Purpura (HSP) was made. There was mild improvement in renal function and complete resolution of rash with no subsequent episodes of gastrointestinal bleeding. The patient was discharged to home on azathioprine therapy and has been asymptomatic to date.

HSP is an IgA-mediated vasculitis characterized by gastrointestinal tract, kidney, skin and joint involvement. Gastrointestinal symptoms may precede cutaneous findings up to 40% of the time. Since the incidence of HSP in the adult population is rare, there may be a delay in diagnosis especially in the absence of skin manifestations. Typical and well-described endoscopic manifestations of HSP include duodenal erosions, ulcerations and hemorrhages.

There are very few reported cases of jejunal ulcerations as the cause of gastrointestinal bleeding. To date, there have been only five reports of ascites as a manifestation of HSP in the adult population. Recognition of diffuse jejunal ulcerations, with or without ascites, should raise clinical suspicion for HSP so that appropriate treatment can be initiated in a timely fashion.

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### Endoscopic Ultrasound (EUS) Findings in Tropical Pancreatitis

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**Introduction:** Tropical Pancreatitis (TP) is an idiopathic Chronic Pancreatitis (CP) unique to nonindustrialized countries. Large intraductal calculi, marked dilatation of the main pancreatic duct, and gland atrophy, characterize it. This is the first report describing Endoscopic Ultrasound (EUS) features.

**Case:** A 26 YOF recently arrived from South India, presented with epigastric pain radiating to the back, nausea and vomiting of 5 days duration. She has had similar episodes since age 15. They usually resolve within 4–5 days with restricting diet, antiemetics and painkillers. Previous EGD showed duodenitis and she was treated for *H. Pylori*. There was minimal ETOH use and no family history of a similar condition or of GI malignancies. Lipase was 87. Triglyceride levels were normal. CT scan of the abdomen showed an ill-defined pancreas with surrounding inflammatory changes, a dilated pancreatic duct, and multiple calcifications. EUS of the pancreas showed parenchymal calcifications, hyperechoic strands, hyperechoic foci, lobularity, and cysts. The pancreatic duct was dilated, up to 6 mm, with hyperechoic walls, visible side branches, with a tortuous/ecstatic appearance.

**Discussion:** EUS is increasingly being utilized to diagnose diseases of the pancreas; including CP. EUS features of CP are echogenic foci, strands, lobularity, cysts, stones, duct dilatation, duct irregularity, hyperechoic duct margins, and visible side branches. These features were all present in our patient, consistent with CP.

TP, first described by Geervarghese, as a disease with pain during childhood, diabetes during puberty, and with death occurring at the prime of life. It initially was thought to be restricted to areas within 30° of latitude from the equator. More than 90% of patients have the illness before 40 years. The overall prevalence in an endemic area is 1 in 500 to 1 in 800 in Southern India. Endocrine insufficiency is an inevitable consequence. The pathophysiology of TP is unknown. Genetic mutations of the *SPINK1* gene, particularly the N34S missense mutation, are seen in up to 50%.

**Conclusion:** EUS features of TP are similar to those of CP, in our patient, who demonstrated all 9 features.[figure1]



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**Small Bowel Metastasis from Lung Cancer**

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**Introduction:** Symptomatic small bowel metastasis from primary carcinoma of the lung is considered a rare clinical entity. We report two distinct clinical presentations of non-small-cell lung carcinoma with gastrointestinal involvement.

**Case 1:** A 68 year old Hispanic male with a non-small-cell lung cancer presented to the ED with shortness of breath, fatigue, anorexia, emesis, and dark stools. Physical examination revealed a pale elderly male, with epigastric fullness and crepitations in the right lung field. Laboratory tests suggested severe anemia with Hemoglobin level of 5.2 gm/dl. Upper endoscopy and colonoscopy failed to identify the etiology of the anemia. CT scan suggested a filling defect in the jejunum with suspected intussusception, requiring partial small bowel resection. Histopathology confirmed malignancy consistent with metastasis from the primary non-small-cell lung carcinoma. He deteriorated clinically with worsening metastasis and died within a few weeks.

**Case 2:** A 74 year old Hispanic male presented with left knee pain. He had anorexia, weight loss, fatigue and occasional dark stools. Physical examination revealed a pale elderly male with tachycardia. His hemoglobin was 7.7 gm/dl with fecal occult blood positive. Endoscopies revealed raised, friable, vascular, superficially ulcerated mucosal lesions in the stomach, jejunum, cecum and rectum. CT scan of the chest was noted for 6 cm size right lower lobe lung mass. There was evidence of extensive bone metastasis. Histopathology report from gastrointestinal lesions revealed large cell poorly differentiated carcinoma. He opted for hospice care and died within a few weeks.

**Discussion:** Cancers of the lung often disseminate early, but small bowel metastasis of a primary lung carcinoma is rarely encountered, with a reported incidence of 0.5% in one series. Large cell carcinoma is the most common histopathologic type. Usual presentation includes intestinal obstruction, perforation and rarely bleeding and peritonitis. Surgical resection may be pursued in patients with excellent primary tumor control in the absence of concurrent other metastatic involvement. The prognosis for patients with small bowel metastasis of non-small-cell lung carcinoma is poor with reported survival ranging from weeks to months.

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**Medical Management of Jejunal Diverticulitis**

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**Case Report:** A 79 year-old woman with cardiac and renal disease was transferred to St. Marys Hospital for intra-abdominal abscesses. She complained of left lower quadrant abdominal pain and two weeks of fever and chills. Abdominal CT demonstrated two abscesses, one 5 cm, interspersed between small bowel loops and anterior to the left kidney and a second, 3.5 cm, anterior to the descending colon at the level of the pelvic brim. On transfer, she was afebrile with normal bowel sounds. She was tender in the left periumbilical region without rebound or guarding. Rectal exam was normal. Leukocyte count was normal. Hemoglobin was 9.6 g/dL. CT of the abdomen repeated three days later showed multiple jejunal diverticula with two abscesses in the jejunal mesentery. The superior collection had decreased in size and the inferior collection was stable, both measuring 4 cm.

She completed a 14-day course of metronidazole and levofloxacin. Twenty-one days later, she was asymptomatic and CT of the abdomen revealed resolution of the superior abscess with a thin-walled diverticulum. The inferior abscess was markedly decreased in size with residual diverticular wall thickening and adjacent soft tissue infiltration. At one month, the patient re-

mained asymptomatic and follow-up CT abdomen at eight months revealed no evidence of abscess.

**Discussion:** Jejunal diverticulosis has been reported to be found in 4.6% of autopsy specimens<sup>1</sup>. Patients can present with chronic complaints or acute complications including diverticulitis with perforation and abscess formation. Acute jejunal diverticulitis occurs in up to 6.4% of patients with diverticulosis<sup>2</sup>. Most cases of jejunal diverticulitis have been treated with surgical resection<sup>2</sup>, but there are a limited number of reported cases of patients with abscess treated non-surgically<sup>3</sup>. In our patient, who presented with diverticulitis with two areas of abscess formation, resolution of symptoms and CT findings occurred with conservative treatment alone. Based on the outcome of our patient, surgery may be avoided when jejunal diverticulitis with abscess is detected early with institution of conservative measures.<sup>1</sup> Noer T. Non-Meckelian Diverticula of the Small Bowel. *Acta Chir Scand* 1960; 120: 175-179. <sup>2</sup>Palder SB, Frey CB. Jejunal Diverticulosis. *Arch Surg* 1988; 123: 889-894. <sup>3</sup>Novak JS, Tobias J, Barkin JS. Nonsurgical Management of Acute Jejunal Diverticulitis: A Review. *Am J Gastroenterol* 1997; 92: 1929-1931.

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**Mystery in the Desert**

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A 74 yo caucasian male from Phoenix, AZ presents with one month of abdominal pain, diarrhea and anorexia. He was recently evaluated at the VA and thought to have a stricture from diverticulitis. His symptoms continued and he presented to Mayo for further evaluation. He had a history of hypertension and diabetes and continued to smoke. His family history was non-contributory. His vital signs were stable and his only physical exam finding was a palpable mass in the abdomen. His labs showed anemia, thrombocytosis and hyperglycemia. His initial CT scan showed an 8 cm infiltrating mass in the sigmoid colon. The differential diagnosis included neoplasm, lymphoma or abscess. A colonoscopy was then attempted but could not be completed secondary to a 5 mm stricture. The patient was then referred to surgery. The lesion was removed successfully. The lesion was adherent to the jejunum, spleen and abdominal side wall. The pathology from the specimen showed a palisading pattern of histiocytes with a center of hyphal elements surrounded by a ring of immunoglobulins. This pattern is known as the Splendore-Hoeppli phenomenon and is highly suggestive of an infection from *Basidiobolus ranarum*, an environmental saprophyte normally found in subtropical climates. It normally causes subcutaneous infection and visceral involvement is rare. However, there have been 15 cases of gastrointestinal basidiobolus diagnosed in Arizona since 1994. The diagnosis usually requires culture, however it can be made by serology or histology. Treatment requires surgical resection and prolonged antifungal therapy. This patient required three months of therapy with itraconazole and did well in follow up.

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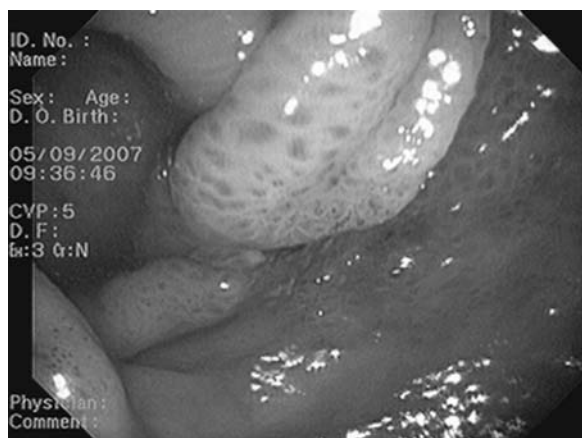
**Infectious Colitis Mimicking Crohn's Disease**

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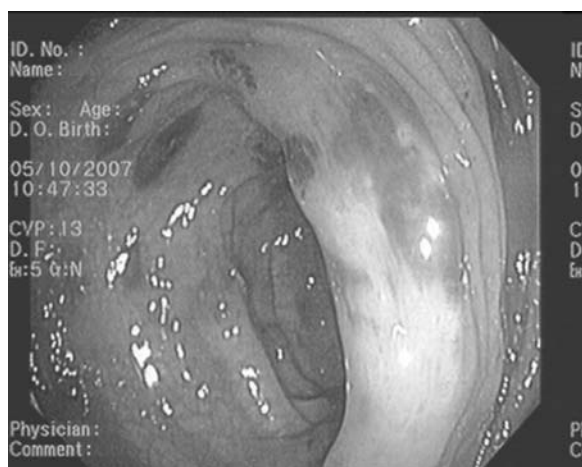
There have been rare case reports of infectious diarrhea mimicking Crohn's disease. We present two cases of infectious colitis in which the endoscopic and radiographic features, and in one case, biopsies, mimic Crohn's disease.

**Case #1:** A 46 year-old woman presented with 4 days of bloody diarrhea up to 10 times a day and lower abdominal cramps, nausea, and vomiting. She was afebrile and had mild tenderness in her right upper abdomen. She had a normal WBC and a HCT of 27. Multiple stool cultures, including for *C.*

difficile, and ova and parasite tests were negative. CT scan showed diffuse colitis from the sigmoid to the cecum with pericolonic infiltrative changes. Colonoscopy revealed patchy erythema, edema, and ulcers in the cecum and the ascending colon. She was started on mesalamine and IV steroids, as well as antibiotics. Colon biopsies revealed just mucosal erosions. Viral stool cultures were ordered, and were positive for adenovirus.[figure1]



**Case #2:** A 34 year-old man presented with 6 days of nausea, vomiting, and diarrhea up to 15 times a day, with fevers and chills. WBC was normal, fecal leukocytes were >20, and stool cultures were negative. Abdominal CT revealed thickening and stranding around the right colon and terminal ileum. Colonoscopy revealed edema, erythema, and petechiae in a patchy distribution from the rectum to the cecum. A small superficial ulcer was seen in the rectum. The patient was started on mesalamine and antibiotics. Biopsies revealed active, chronic inflammation in the terminal ileum and colon, with glandular architectural distortion. Blood cultures were positive for Salmonella.[figure2]



**Discussion:** These two cases highlight the rare, but very real, possibilities of infectious colitis mimicking Crohn's disease. These would seem to favor delaying steroids and other aggressive options considered in the "top-down" approach until infectious etiologies are ruled out.

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**Introduction:** Elevations of serum lipase can be seen in pancreatitis and less commonly in cholecystitis, bowel ischemia, renal insufficiency, hepatic dysfunction, alcohol abuse, intracranial events, sarcoidosis, macro-lipaseemia, IBD and prolonged ICU stay. We describe a patient with a prior history of acute pancreatitis and a chronically elevated serum lipase caused by a sub-centimeter pancreatic neuroendocrine tumor (P-NET) diagnosed by EUS-FNA.

**Case Summary:** A sixty-three year old black female with a past medical history significant for hypertension and glaucoma presented after a recent hospitalization for an acute bout of pancreatitis with subsequent persistence of abdominal pain, bloating and a chronically elevated lipase. The patient denied recent history of blunt trauma, weight loss, nausea, vomiting or diarrhea. Physical exam was unremarkable. Laboratory evaluation revealed an elevated serum lipase level of 517 U/L ( $4 \times$  ULN) while amylase, complete blood count and comprehensive metabolic panel were within normal limits. An abdominal ultrasound, computerized tomography with pancreatic protocol and magnetic resonance imaging with cholangiopancreatography, and chest x-ray were normal. Repeated lipase levels over the subsequent three months confirmed persistent elevation ranging from 3–5  $\times$  ULN. An endoscopic ultrasound was performed which revealed a 5 mm, round, hypoechoic mass in the neck of the pancreas. The main pancreatic duct was within normal limits and not compressed by the lesion. Fine needle aspiration of the mass was performed with cytology favoring a neuroendocrine tumor versus well-differentiated adenocarcinoma. This diagnosis was confirmed by a second pathologist. Chromogranin A, insulin, VIP and glucagon levels as well as an octreotide scan were all within normal limits.

**Conclusion:** Elevated serum lipase in a patient without radiographic or clinical signs of pancreatitis can be a diagnostic dilemma. Lipase levels above three to five times the upper limit of normal are more specific and suggest a pancreatic source. Our patient had a history of pancreatitis and a persistent lipase of four to five times the upper limit of normal which was likely caused by tumor compression of a small pancreatic side branch duct. The lesion was beyond the sensitivity of CT or MRI and visualized only by endoscopic ultrasound. Our case suggests that EUS should be considered in patients with an isolated, elevated level of lipase when no other cause is identified.

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### **Uncommon Presentation of PTLD in the Esophagus**

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75 year-old man with diffuse B-cell lymphoma was found to have new thickening of mid-esophagus on a CT. Questioning revealed progressive solid/liquid dysphagia. GI was consulted.

Patient underwent kidney transplant 1 yr ago. Approx. 5 mths later, he presented with abd. pain and weight loss. CT revealed 2 mesenteric lesions and multiple small nodules in liver, spleen, and lung bases. Lung biopsy revealed diffuse B-cell lymphoma, EBV+. Patient was diagnosed with post-transplant lymphoproliferative disorder (PTLD). Immunosuppressive medications were tapered.

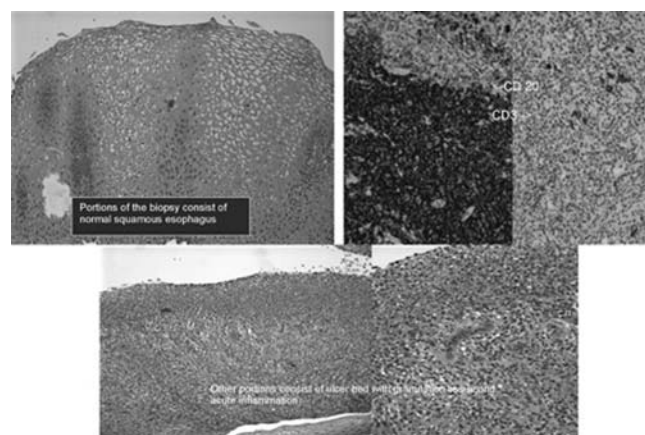
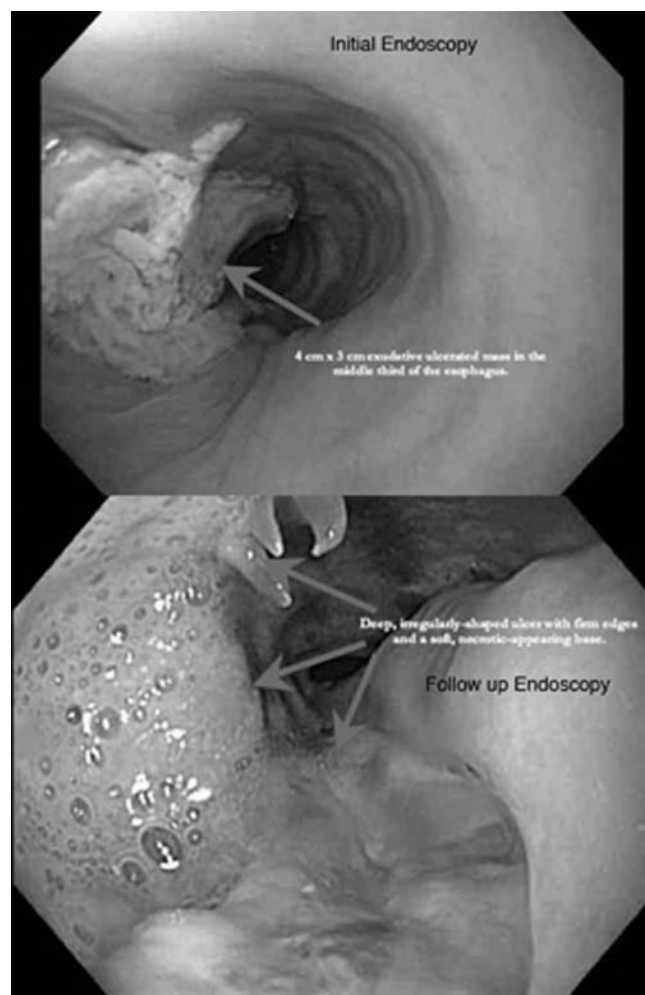
On day of admission, pt. developed acute mental status changes. Imaging revealed progression of brain lesions. Chest CT revealed new thickening of mid-esophagus prompting GI consultation.

Upper endoscopy showed a  $4 \times 3$  cm ulcerated mass in middle third of esophagus. Fig. 1. Path showed necrotic debris, bacteria, and inflammatory cells. Sirolimus was discontinued and repeat endoscopy planned. 6 wks later, CT chest showed  $39 \times 31$  mm necrotic mass in the middle mediastinum. Patient developed worsening dysphagia, odynophagia and coughing. Ba esophagram showed extraluminal flow of contrast in mid third of esophagus. This cavity measured  $4 \times 1 \times 1.8$  cm.

Upper endoscopy was repeated. Fig. 1.

Pathology. Fig. 2. Ulcer with subadjacent B-cell neoplasm consistent with PTLD. Stains for CD20 and CD3 confirmatory.

PEG tube was placed for nutritional support. Rituximab was considered, however given overall poor prognosis the patient opted for hospice care. PTLTD should always be suspected in patients with solid organ transplantation. GI tract involvement provides an opportunity for endoscopic diagnosis. The unique aspect of this case is the esophageal presentation after kidney transplant in an adult. Most case reports in literature are of pediatric patients with liver, intestinal, lung or heart transplantation with PTLTD affecting the colon, small bowel or stomach.[figure1][figure2]



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### Fusobacterium Nucleatum: An Uncommon Cause of Pyogenic Liver Abscess

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A 35 year old previously healthy African American male presented with recurrent fevers, chills, and diffuse abdominal pain for 3 weeks. He denied any nausea, vomiting, diarrhea, or recent travel. Physical exam was significant for a temperature of 38.7 C, mild epigastric and right upper quadrant tenderness without rebound or guarding, and a normal liver span. Laboratory data indicated a leukocyte count of 13,700 and minimally elevated alkaline phosphatase. CT scan of the abdomen revealed a 9 cm x 5.1 cm abscess in the right hepatic lobe. Entamoeba histolytica serologies, blood cultures, and a HIV test were all negative. The patient underwent CT guided percutaneous aspiration of the abscess with drainage placement. He was started empirically on ampicillin/sulbactam awaiting culture results, which eventually grew *Fusobacterium nucleatum*. Repeat CT scans revealed that the abscess was diminishing in size. He was subsequently discharged on amoxicillin/clavulanate to complete 6 weeks of therapy. Additional history later revealed that he had a routine dental cleaning 2 weeks prior to initiation of his symptoms.

The majority of pyogenic liver abscesses are the result of contiguous spread from infections in the biliary tree or peritoneal cavity while a much smaller number involve hematogenous seeding of the liver. The most common pathogens are mixed facultative and anaerobic gastrointestinal flora with *E. coli* and *Klebsiella pneumoniae* being the most frequently isolated. *Fusobacterium nucleatum* is an anaerobic Gram negative rod that is part of the oral flora and typically causes only dental and upper respiratory tract infections. It is not commonly associated with hepatic abscesses. In this case, the patient likely had a transient bacteremia from his recent dental cleaning that seeded the liver. This case illustrates the importance not only of obtaining a thorough history but also the importance of covering for anaerobic bacteria in intraabdominal abscesses. Although *Fusobacterium nucleatum* is a rare cause of hepatic abscesses, it and other anaerobes should be considered in patients who have undergone recent dental work.

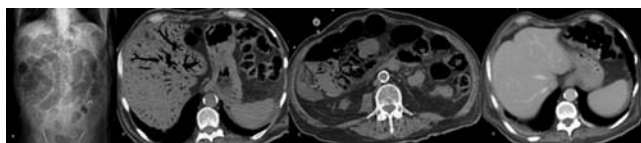
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### Extensive Portal Venous Gas and Pneumatosis Intestinalis in the Absence of Small Bowel Ischemia or Infarction

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Portal venous gas and pneumatosis intestinalis are usually associated with transmural small bowel ischemia or infarction and are generally fatal. We present here a case with negative laparotomy and successful outcome.

A 66 y male with multiple co-morbidities like hypertension, diabetes, coronary artery disease, advanced COPD, who was a recent hospital discharge following bronchopneumonia and respiratory failure, presented to the ER with sudden severe abdominal pain. On clinical examination he had frank signs of peritonitis. He had leukocytosis with bandemia (21%). An abdominal CT showed extensive pneumatosis intestinalis and portal venous gas (Fig. 1A-C). He was resuscitated and taken up for emergency laparotomy. Per op there was no evidence of any bowel ischemia, infarction or perforation. Diffuse pneumatosis was noted throughout the small intestine. Mesenteric pulses were well palpable. Colon, Liver and gall bladder were normal. He was managed in ICU, initially with TPN and 2 weeks later he was initiated on tube feeding. He gradually recovered and was discharged. Repeat CT scan showed complete resolution of portal venous gas and pneumatosis (Fig. 1D). Portal venous gas and pneumatosis intestinalis generally denote mesenteric ischemia with grave prognosis. Patients with negative laparotomy are likely to recover uneventfully.[figure1]



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### Massive Pleural Effusion as Initial Presentation of Advanced Liver Cirrhosis

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Hepatic hydrothorax is seen in 5–10% of patients diagnosed with liver cirrhosis, and is rarely present in the absence of ascites. The diagnosis is considered in the presence of a pleural effusion in a cirrhotic patient without pulmonary or cardiac disease.

A 24-year-old woman without history of prior liver disease developed a massive exudative right pleural effusion that required a tube thoracostomy for a suspected pneumonic process with associated effusion. The patient required a second intervention and chest tube placement. An extensive work up failed to find the etiology of the effusion, but revealed altered liver function tests, increased CA-125 and Ca 19-9 tumor markers and a positive hepatitis C virus antibody with ongoing viral replication. Imaging revealed hepatosplenomegaly without ascites. Fluid analysis evolved from an exudate to a transudate and alerted to the possibility of a hepatic hydrothorax. Rapid transit of fluid from the abdominal cavity to the right lung was demonstrated using Tc-<sup>99</sup> sulfur colloid. An *Enterococcus fecalis* was recovered from the fluid. Salt restriction and aggressive diuresis decreased the thoracostomy output, but she developed massive ascites once the tube was removed suggesting closure of the hemi-diaphragm porus connections. Ascites was refractory to medical treatment. A Transjugular intrahepatic porto-systemic shunt was successful in decreasing portal vein pressure from 16 to 6 mm Hg, and the patient is undergoing evaluation for a liver transplant.

A massive pleural effusion led to the diagnosis of chronic liver disease associated to hepatitis C in this patient. Hepatic hydrothorax from porous diaphragm syndrome was a therapeutic challenge in this young female with no prior history of liver disease or ascites. Radiotracer study confirmed a peritoneal origin of the fluid. Spontaneous bacterial empyema has been reported and could explain the initial fluid findings. In addition, tumor markers CA 19-9, CA-125, which have been reported increased with liver fibrosis, were helpful in suggesting the presence of cirrhosis or advanced fibrosis accounting for her clinical presentation.

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### Severe Copper Deficiency in a Patient with History of Gastric Bypass Leading to CNS Demyelination, Severe Ataxia and Peripheral Neuropathy

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Copper is an essential micronutrient necessary for the hematologic and neurologic systems. Acquired copper deficiency in humans has been described, causing a syndrome similar to the subacute combined degeneration of vitamin B<sub>12</sub> deficiency. Copper deficiency is being increasingly recognized in adult populations due to various causes including high zinc levels, copper chelating agents and after gastric bypass surgery. We present a case patient with severe hypocupremia leading to profound neurological symptoms to stress the importance of this clinical entity and its early diagnosis and treatment. We present a 52 year-old white male who had Roux-en-Y gastric bypass surgery. He was maintained on multivitamin supplements including Vitamin B<sub>12</sub>, iron and zinc. Fifteen years after his gastric bypass he started having worsening sensory ataxia and worsening paresthesias of

the lower extremities, and was hospitalized for severe weakness in his lower extremities. On admission his nutritional evaluation revealed normal serum levels for Vitamin B<sub>12</sub>, zinc and iron. However he was found to have an extremely low serum copper level. MRI of the spine showed T-2 hyperintensity within the dorsal spinal cord from C2 through C5 which has been described in patients with copper deficiency. The patient was started on copper supplements, showed significant clinical improvement, and was maintained on copper supplements after his discharge. Copper deficiency is a rare complication following gastric bypass surgery. Copper is primarily absorbed from stomach and proximal small bowel. It is not clear why copper deficiency occurs in some but not all patients after gastric surgery. Iron and zinc have been described to inhibit copper uptake in the proximal bowel. Zinc and copper compete for absorption in the digestive tract so that a diet that is excessive in one of these minerals may result in a deficiency in the other. Bariatric procedures such as gastric bypass surgery result in a similar functional anatomy of the proximal gut and may place more patients at increased risk of copper deficiency. Early recognition and therapy with copper supplements may lead to a decrease in both neurologic and other known hematologic consequences of hypocupremia. Oral copper should be taken in a different time preferably earlier to the oral multivitamins or oral zinc to prevent the chelating effect of zinc on copper.

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### Benign Small Bowel Thickening with Lymphadenopathy: A Manifestation of Celiac Disease

Jerry Martel, MD, MPH, Daniel A. Sussman, MD, Robert I. Goldberg, MD, Jamie S. Barkin, MD\*. Division of Gastroenterology, University of Miami Miller School of Medicine, Miami, FL and Division of Gastroenterology, Mount Sinai Medical Center, Miami Beach, FL.

**Introduction:** Celiac disease (CD) is the most common inheritable GI disorder with an overall prevalence of 1:250. Small bowel lymphoma with lymphadenopathy is a well-documented entity complicating the clinical course of patients with CD. This accounts for one-half to two-thirds of malignancies associated with CD. However, small bowel thickening with lymphadenopathy does not always represent malignancy.

**Aim:** The aim of these case reports is to present small bowel thickening and lymphadenopathy on CT scan as an unusual part of the spectrum of CD.

**Table 1.**

Patient Information	Patient A	Patient B
Age, Sex, Presentation	40 y/o woman with abdominal pain and diarrhea	76 y/o man with weight loss and diarrhea
CT Scan Reported Findings	Multiple prominent lymph nodes in left abdominal mesentery; Small bowel thickening with partial transient intussusception	Mild mesenteric lymphadenopathy and thickening of a portion of the small bowel
Diagnostic Modality Biopsy Results	Diagnostic Laparoscopy Reactive lymphoid hyperplasia with small intestinal mucosa with mild villous blunting and striking intraepithelial lymphocytosis	Enteroscopy & Biopsy Intestinal mucosa with complete blunting of villi with increased surface epithelial lymphocytes consistent with sprue
Positive Serologies Management	IgA TTG Gluten-free Diet	IgA antiendomysial Ab Gluten-free diet & Prednisone

**Discussion:** Only one prior case is reported in the literature presenting with small bowel thickening and lymphadenopathy of benign etiology in a patient with CD. We report two patients who presented with CT findings of small bowel thickening and mesenteric lymphadenopathy. (Table A). The patients have CD confirmed by biopsy and/or serologies. The benign nature of thickening and lymphadenopathy was confirmed by laparoscopic biopsy in one case and endoscopic biopsy with clinical and imaging follow-up in the other. Upon initiation of celiac treatment, the patients had clinical improvement, reversion of their small bowel thickening, and regression of their lymphadenopathy.

**Conclusion:** Small bowel thickening and mesenteric lymphadenopathy may be the initial finding of CD and may be of a benign etiology.

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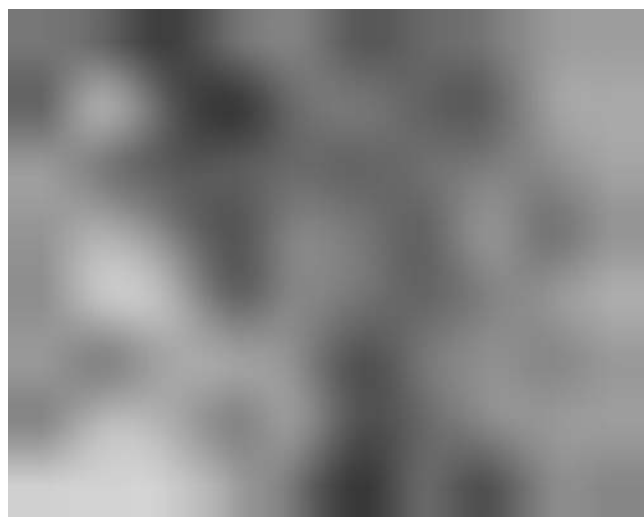
### A Case of Metastatic Adenocarcinoma Presenting with Fulminant Hepatic Failure and Elevated Alpha Fetoprotein Level

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Fulminant hepatic failure (FHF) most commonly occurs due to viral hepatitis or drug toxicity and rarely occurs as the initial presentation of malignancy. We report the case of a patient without prior history of malignancy who presented with FHF, was found to have metastatic adenocarcinoma and interestingly, had a very high alpha fetoprotein (AFP) level.

A 59 year old woman was admitted with progressive jaundice, abdominal pain, ascites, and lower extremity edema. She denied any new medications, alcohol or drug use. Laboratory data revealed alkaline phosphatase of 1279 IU/L, alanine aminotransferase of 88 IU/L, aspartate aminotransferase of 280 IU/L, total bilirubin 5.4 mg/dl, low albumin, and prolonged prothrombin time. No etiology for FHF was apparent on initial evaluation including ultrasound.

Serum AFP and carcinoembryonic antigen (CEA) were elevated at 1439 ng/ml and 9.3 ng/ml respectively. Liver biopsy revealed moderately differentiated adenocarcinoma arising from the gastrointestinal tract, most likely of colonic origin. [figure1]Unenhanced CT scan at the time of biopsy revealed metastatic disease.[figure2]Unfortunately, the patient's condition deteriorated and she died 9 days after admission.



A review of the literature revealed initial presentation of FHF due to metastatic cancer to be rare and reported cases were primarily diagnosed at autopsy. The clinical presentation and laboratory findings are non-specific. Although primarily used to aid in the diagnosis of hepatocellular carcinomas and yolk sac tumors, elevated AFP levels have been rarely reported in



gastrointestinal malignancies. Mortality rates are high and treatment options are limited, especially since liver transplantation is contraindicated.

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### Ischemic Hepatitis Arising in the Setting of Hitherto Undiagnosed Cirrhosis Secondary to Hemochromatosis

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Ischemic hepatitis (IH) is characterized by an abrupt, marked but reversible increase in serum aminotransferase concentration(s) arising within a clinical setting of circulatory failure and systolic hypotension, in which other possible causes of hepatocellular necrosis can be excluded reliably. The histological hallmarks are centrilobular hepatocyte necrosis, central vein congestion and distortion of adjacent hepatic sinusoids. Prompt recovery may follow but the overall course is governed by underlying disease. It is unclear if the presence of end-stage liver disease (ESLD), whether as the result of hepatic congestion or otherwise, predisposes patients to develop IH more readily.

A 45 year-old man with non-ischemic cardiomyopathy was transferred for management of cardiogenic shock. He was intubated, and had an intra-aortic balloon pump *in situ*. Despite inotropic support he remained hypotensive (mean BP: 82/46 mm Hg). Physical examination demonstrated no external evidence of ESLD. Laboratory data were as follows: aspartate aminotransferase 1860 IU/L (normal range [NR]: 10–60), alanine aminotransferase 1494 IU/L (NR: 10–60), prothrombin time 23.8 s (11.1–13.1) and total serum bilirubin 2.3 mg% (NR: 0.2–1.2). Acute hepatitis A, B and C virus infections were excluded on the basis of appropriate serologic testing. His antinuclear antibody titer was weakly positive (1:40). The serum ceruloplasmin concentration was 39 mg% (NR: 20–60). His serum ferritin concentration was 7774 ng/mL (NR: 30–300), and the iron saturation 68% (NR: 14–50). Liver histology revealed cirrhosis (Masson trichrome stain), and grade 4/4 iron overload involving hepatocytes, Kupffer cells and the biliary epithelium (Prussian blue iron stain). In some centrilobular areas prior hepatocyte loss consistent with ischemic injury was evident, but not chronic passive congestion. Testing for the commonest mutations in the hemochromatosis (HC) gene was negative. Despite improvement in liver tests with further supportive care, he developed renal dysfunction. Continued systolic hypotension precluded hemodialysis, and the patient died 21 days after transfer from complications of ESLD.

This man's clinical and laboratory picture at the time of transfer was entirely consistent with IH. However, cirrhosis secondary to HC was the dominant histologic abnormality, almost totally obscuring changes of IH. The diagnosis of HC, although unexpected, was important so as to avoid unnecessary efforts at cardiac transplant evaluation.



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### Unusual Complication of a Colonic Interposition with an Unusual Solution

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A 30 year old woman underwent an esophagectomy with colonic interposition for management of lye induced esophageal stricture. Unfortunately, the surgery was complicated by recalcitrant stricture at both the esophago-colonic and colo-gastric anastomoses. These esophageal strictures have been managed with multiple dilations (approximately once a month) using a Savary-Gilliard systems as well as needle knife stricturoplasty and injection of steroids into the lesion. However, the stricture at the colo-gastric anastomosis persisted. This was most recently managed with placement of a 12 cm long by 25 mm wide Polyflex stent (Boston Scientific, Natick MA) to achieve tissue re-modeling at the anastomosis site. Prior to assembly of the stent, a non-absorbable suture was affixed through the proximal aspect of the stent. This was anchored to the colonic mucosa proximal to the anastomosis using a resolution clip (Boston Scientific, Natick MA) to prevent early distal migration. Two weeks later the Polyflex stent migrated distally into the stomach. This was extracted using a rat-toothed forceps and standard endoscopy. Since the stent was extracted nine months ago she has done well and not required any more dilation.

**Discussion:** Approximately 5000 caustic ingestions occur annually in the United States and is the leading cause of esophageal strictures in the pediatric population. Urgent upper endoscopy is recommended to assess the degree of mucosal injury which has a bearing on immediate management as well as prognosis. Up to one-third of patients develop esophageal strictures usually in those with severe mucosal injury. Although management of caustic strictures usually requires multiple sessions of esophageal dilations, temporary placement of self expanding plastic stents (SEPS) has also been successful in case series. In patients with refractory esophageal strictures, esophagectomy with colonic interposition may be required. To our knowledge this is the first case of a Polyflex stent placement with successful resolution of a colo-gastric anastomotic stricture. VIDEO and IMAGES available for presentation.

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### Pancreatic Cysts in a Patient with Von Hippel-Lindau Disease Causing Common Bile Duct Obstruction

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Von Hippel-Lindau Disease (VHL) is characterized by the formation of multiple vascular tumors (primarily in the CNS) in response to the uninhibited action of hypoxia inducible factor (HIF). Normally an adaptive response to ischemia, HIF is regulated by the VHL protein. In individuals with mutations in both genes coding for the VHL protein, there is unregulated action of HIF with subsequent angiogenesis and tumor formation. Among other complications of VHL are pancreatic tumors and cysts. Though pancreatic lesions reportedly occur in up to 77% of VHL patients, symptoms are rare. We present a patient with VHL who developed CBD compression and obstructive jaundice requiring ERCP and stent placement due to diffuse cystic involvement of the pancreas.

**Case:** A 37 yo woman with no previous history presented to another facility with ataxia, dysphagia and headache. After a CT scan revealed two vascular cerebellar lesions, consistent with hemangioblastomas, the patient was transferred to our institution for arterial embolization. Her stay was prolonged by post surgical complications. While recovering, she developed abdominal pain and cholestatic jaundice. Abdominal ultrasonography showed intra- and extra-hepatic biliary ductal dilation, a CBD diameter of 13 mm and multiple cystic lesions in the pancreas. The patient developed fever and leukocytosis, and then underwent an ERCP. The cholangiogram revealed a distal CBD stricture, with obtuse angles suggestive of extrinsic bile duct compression. Brushings of the stricture for histology revealed degenerative bile duct cells

and no evidence of malignancy. The stricture was managed with a graduated dilating catheter and a 10 fr stent was placed, which resulted in rapid endoscopically apparent drainage of the biliary tree. The patient's symptoms and liver tests improved and she was discharged to a rehab facility.

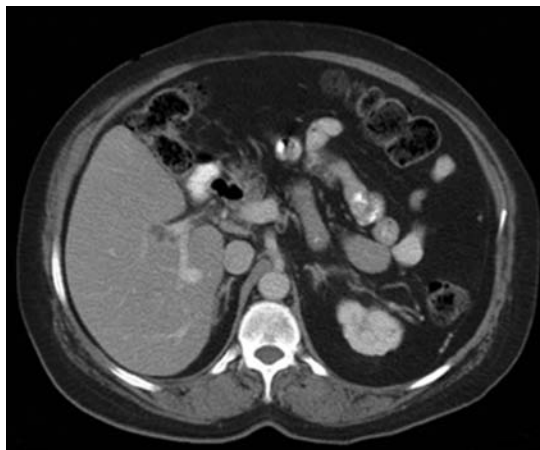
**Comment:** Pancreatic lesions can be common in VHL (depending on the family and genetic mutation studied). The most common lesions found in VHL are simple cysts, serous cystadenomas, and neuroendocrine tumors, but adenocarcinoma, metastatic renal carcinoma, and hemangiomas have all been reported. While early satiety and pain from pancreatic cysts occur, CBD obstruction from external compression by a pancreatic cyst in VHL is extremely rare. In summary, this was an unusual case of VHL with pancreatic cystic lesions causing extrinsic biliary obstruction, which was able to be palliated with ERCP and stent placement.

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### Spontaneous Choledochoduodenal Fistula in a 64 Year Old Lady with a Remote History of Cholecystectomy

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We report the case of a 64-year-old Hispanic lady with h/cholecystectomy 10 years ago who presented with intermittent abdominal pain ever since then. The abdominal pain was described as aching in quality, epigastric in location and radiated up to the right shoulder and back. She has had nausea but no vomiting, fevers or chills. Past medical history was significant for hypertension, dyslipidemia and choledocholithiasis. Her medications included ursodiol, esomeprazole, verapamil, amitriptyline, and aspirin. There was no history of substance abuse or NSAID intake or duodenal ulcer. Physical examination was within normal limits except for diffuse tenderness in the epigastric region with no guarding or rebound tenderness. CT of the abdomen showed a moderate amount of air within the intrahepatic biliary system with mild dilation of the intrahepatic ducts with extension of the dilation to an even more dilated extrahepatic duct, which measured 2.5 cm in its maximal AP dimension. Multiple foci of air consistent with pneumobilia were identified. ERCP, occluded cholangiogram as well as EGD were done which showed a fistula of 7-8 mm in diameter from the upper third of the main bile duct into the duodenal bulb. The symptoms of the patient were attributed to this fistula, as a result of ingested food going into her bile duct. Clipping of the fistula via ERCP, though attempted, was unsuccessful and hence a choledochojunostomy with Roux-En-Y loop was performed. The post operative course was uneventful with the patient reporting no symptoms in a 1 year follow-up period. Bilioenteric fistulae are usually incidental findings and arise as a complication of chronic duodenal ulcer disease, cholelithiasis, previous instrumentation to the biliary system or malignancy. The presence





of a fistula by itself does not equate to necessity for surgery and treatment of the uncomplicated fistula appears unnecessary.[figure1]

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#### Adult T-Cell Leukemia/Lymphoma with Terminal Ileal Involvement

Biju K. Alex, MD, Atoussa Farough, MD, Roshan M. Bashir, MD\*. Department of Medicine, Washington Hospital Center, Washington, DC.

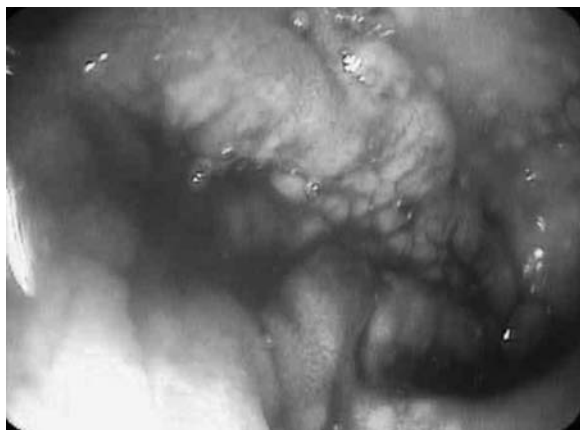
**Introduction:** Adult T-cell leukemia/lymphoma (ATLL) is an uncommon highly aggressive non-hodgkins lymphoma. Secondary gastrointestinal involvement has been documented in literature, predominately the gastrum. This rare case describes a pt with ATLL involving the terminal ileum with endoscopy findings.

**Case Presentation:** The patient is a 64 yo old male from Ghana who was admitted with symptoms of fatigue, weight loss and skin rash  $\times$  1 month. He initially presented 2 wks ago as outpatient with diarrhea and vague abd pain which resolved at the time of admission and denied any acute GI complaints upon presentation. Pt had tender right supraclavicular and b/l nontender cervical lymphadenopathy measured  $2 \times 2$  cm. Abd exam was nontender, nondistended with active bowel sounds. Liver span measured 40 cm and no splenomegaly. On skin exam, there was pruritic scaly hyperkeratotic papules involving the palms, soles, chest, abdomen, back with hyperpigmentation. On laboratory examination he had hypercalcemia and renal insufficiency. Western blot was positive for HTLV1. Skin, bone marrow and lymph node biopsy revealed ATLL.

**Endoscopy Findings:** EGD showed a diffuse congested mucosa with ulcerative lesions in the proximal gastric and fundus. Colonoscopy revealed diffuse mucosal erythema in the sigmoid and descending colon; terminal ileum evaluation demonstrated polypoid mucosa with cobblestone appearance. Biopsies of the colon, terminal ileum and gastric mucosa were all diagnostic of ATLL.

**Discussion:** ATLL is associated with human T-cell lymphotropic virus type I (HTLV-I). HTLV-1 affects 10–20 million people worldwide and carries a life time risk of 2–5% of developing ATLL. GI infiltration with gastrum is more commonly involved with the frequency much lower for large and small intestine.

**Conclusion:** This is a rare case of ATLL involving the terminal ileum. Only two cases of terminal ileal involvement have been described in Japan. It can be suggested that routine endoscopic surveillance of the upper and lower GI tract in all newly diagnosed patients with ATLL is recommended for prognostic purposes and in evaluating response to chemotherapy.[figure1]



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#### Perforated Meckel's Diverticulum Mimicking Crohn's Disease Presenting with Bowel and Urinary Obstruction

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To describe an unusual case of Meckel's diverticulum presenting with combined bowel and urinary obstruction.

All data, including those from patient history, physical examination, laboratory tests, imaging, endoscopy, surgery, and pathology, were obtained in the course of patient care and presented with the consent of the patient.

Meckel's diverticulum is a common congenital anomaly of the gastrointestinal tract, but an uncommon cause of serious complications in adults. While reports of hemorrhage, bowel obstruction, and perforation associated with Meckel's diverticulum exist, there have been no prior reports of combined urinary and bowel obstruction due to abscess formation. We report the case of a 21-year-old man, with history of recurrent papillary thyroid cancer, but no prior abdominal surgery, who presented with a one-month history of rectal pain and new onset obstipation and urinary retention. He reported night sweats and weight loss, and had a second-degree relative with known Crohn's disease. Digital rectal examination was notable for marked tenderness with proximal induration. CT of the abdomen revealed a large, complex, circumferential, perirectal abscess compressing the rectal lumen and base of the urinary bladder, associated with thickening of the terminal ileum and an ileocecal fistula. Flexible sigmoidoscopy with endorectal ultrasound displayed a complex abscess with extensive mucosal and surrounding inflammation. At exploratory laparotomy, a Meckel's diverticulum, with a large perforation at its base, was discovered near the ileocecal fistula and immediately superior to the perirectal abscess. The section of small bowel containing the Meckel's diverticulum, terminal ileum, and cecum were all resected, and the abscess was debrided. No gross or pathologic evidence for malignancy or Crohn's disease was seen. The patient's symptoms resolved post-operatively.

This is the first reported case of a perforated Meckel's diverticulum with secondary pelvic abscess formation and fistulization, mimicking Crohn's disease, presenting with combined bowel and urinary obstruction.

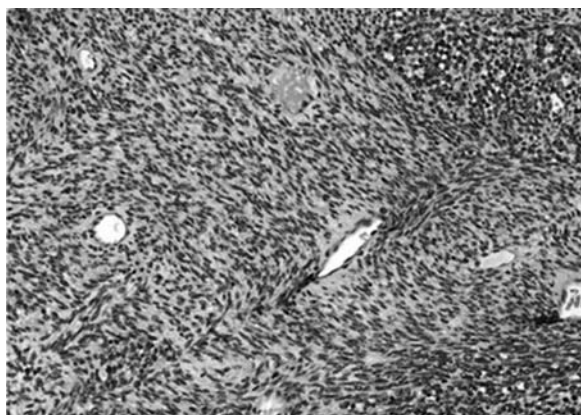
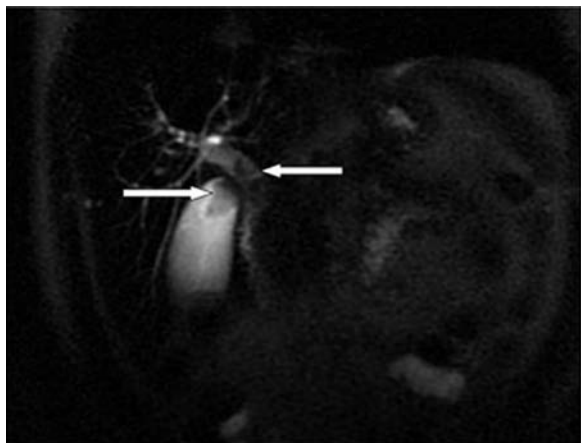
706

#### A Rare Case of Biliary Synovial Sarcoma

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A 51-year-old Hispanic male was referred to our hospital with obstructive jaundice and a possible cholangiocarcinoma. At the other hospital patient had undergone laboratory examination, CT scan and ERCP. Laboratory examination showed leucocytosis, elevated liver function tests (total bilirubin 14 mg/dl, conjugated bilirubin 10 mg/dl, and alkaline phosphatase of 800 U/per liter). Computed tomography (CT) abdomen showed dilated CBD and a mass obstructing the neck of gall bladder. During endoscopic retrograde cholangiopancreatography (ERCP) lots of mucus membrane like material was expressed and sent to histopathology. No definitive pathological diagnosis could be made because of the complexity of the tissue. Patient continued to be symptomatic and had persistently elevated LFTs. After transfer, MRCP with gadolinium revealed an intraluminal mass within the common bile duct with probable extension into the gallbladder, most consistent with cholangiocarcinoma (Fig. 1). Patient underwent Whipple's procedure for this suspicious mass. Gross pathology of the resected specimen revealed two separate unconnected polypoid masses in common bile duct and gall bladder. Histopathology revealed whorls of small darkly staining cells arranged in sheets suggestive of synovial sarcoma vs. small cell carcinoma vs. peripheral neuroectodermal tumor (PNET) (Fig. 2). Various immunohistochemical stains were performed on the tumor specimen (positive for CD 99, Bcl-2 and synatophysin) favoring a poorly differentiated synovial sarcoma. Slides were reviewed with two other pathologists who concurred with the interpretation

of the tumor as synovial sarcoma. To the best of our knowledge this is one of the first rare cases described in literature. Patient was lost to follow-up before initiation of chemotherapy.[figure1][figure2]



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#### Syncope Secondary to the Metastasis of Hepatocellular Carcinoma

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A 73 year old male with history of hemochromatosis and cirrhosis presented after an episode of syncope. He was found to be hypotensive and EKG showed sinus bradycardia. An echocardiogram showed a right atrial mass presumed to represent an atrial myxoma. A CT of the chest (Fig. 1) further demonstrated the mass to be extending through the tricuspid valve into the right ventricle. Prior to excision, a CT of the abdomen was performed (Fig. 2) revealing multiple hepatic hyperdense nodules, suggesting hepatocellular carcinoma. AFP was found to be 1237.5. The patient declined biopsy and therapeutic measures. He returned home with palliative treatment.

Cardiac metastasis is a more common manifestation than is perceived. There is a reported 10% incidence in patients with hepatocellular carcinoma, 0.67%–3% present as an intracavitary lesion. The carcinoma can either invade the IVC with extension into the RA or form a neoplastic thrombus embedding in the cavity.

Two mechanisms have been shown to cause syncope in cases of Cardiac Metastases. Intracavitary lesions may obstruct blood flow via ball valve mechanism or cause tricuspid insufficiency by inhibiting closure of the valve. Echocardiography showed a huge mass in the right ventricle protruding

through the tricuspid valve into the right atrium and keeping it from closing. Color Doppler showed evidence of tricuspid insufficiency and reduced cardiac output, the likely cause of syncope in our patient.

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#### Isolated Neurofibroma of the Pylorus Presenting as “Idiopathic” Gastroparesis, Refractory to Standard Medical Management

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We report a benign isolated neurofibroma of the pylorus resulting in pyloric stenosis, presented with epigastric pain, nausea, vomiting, and severe weight loss. After extensive evaluations patient was diagnosed with idiopathic gastroparesis (IGP), without any response to medical treatment. Remarkable recovery followed implantation of gastric electrical stimulator (GES) with simultaneous resection of serosal nodule (histologically diagnosed with neurofibroma) and pyloroplasty.

A 24 year old male, developed severe diarrhea, nausea, vomiting, and weight loss of 100 lbs over 1 year, following his trip to South America. EGD evaluation showed narrowing of the pylorus addressed with 2 injections of botox. Due to the lack of symptom relief, gastric emptying test (GET), CT scan, SBFT results suggested partial gastric outlet obstruction and enlarged stomach. Exploratory laparoscopies (X2) were inconclusive. Extensive testing for various diseases was negative.

He was referred to us in Nov. 06 for further evaluation of isyptoms of IGP with severe malnutrition. 4 hour GET proved delayed emptying (44% retained at the end of 4 hours; normal: 0–10%). USG of the abdomen and HIDA scan suggested some sludge and cholelithiasis. During this time, patient was treated for GI symptoms with metoclopramide, tegaserod, erythromycin, domperidone, scopolamine patch and desipramine. As the patient continued to lose weight despite oral nutritional supplementation, liquid diet, and presence of GI symptoms it was decided to implant the GES. CT of the abdomen showed a 3 cm intramural mass near the gastric pylorus. Placement of GES, pyloroplasty, J-tube placement, and a cholecystectomy was done in Jan, 07. Intraoperatively, the thickening of the muscle around the pylorus with serosal nodules was found and resected. Pathology report confirmed presence of a neurofibroma, without involvement of peritoneal lymph nodes. Patient was discharged in stable conditions with a good control of his GP-like symptoms. During subsequent follow up visit in April 2007 it was observed that patient regained 70 lbs and he was not in a need for continuous J-tube feeding which was removed at that time. This case is presenting a very complicated and rare clinical condition of isolated neurofibroma of the pylorus which was a challenging task for caring physicians due to the symptoms suggestive of IGP.

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#### Granulocytic (Myeloid) Sarcoma of Stomach Presenting with Upper Gastrointestinal Bleeding

M. Singh, MD, D. Baltodano, MD, C. Zanardi, MD, P. Holtzapple, MD\*. *Gastroenterology, Pathology, SUNY Upstate Medical University, Syracuse, NY.*

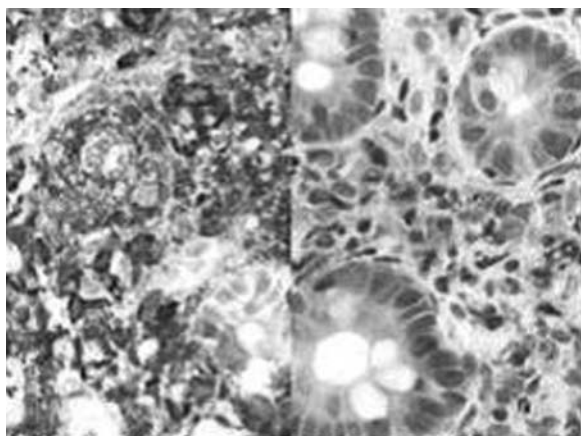
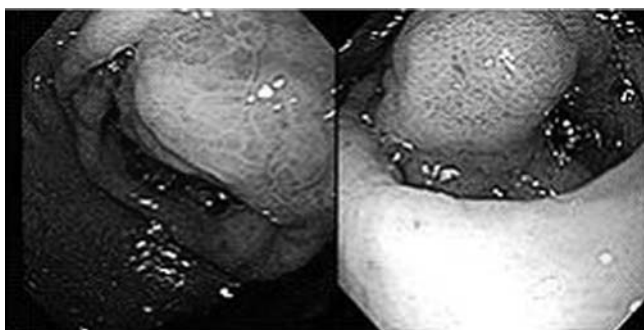
**Introduction:** Granulocytic sarcoma (GS) is a localized extramedullary tumor of neoplastic immature myeloid cells. GS is the “tissue phase” of some forms of myeloid leukemia. We present a patient with upper GI bleed secondary to GS of the stomach.

**Case Summary:** 66 yr/F with myelodysplastic syndrome (MDS) for 18 months presented with dark tarry stools. She received thalidomide and azacytidine therapy but had refractory anemia (RAEB). At admission she was hypotensive, tachycardic with mild abdominal tenderness. Labs show hematocrit of 20, platelets count of 59,000 with WBC count of 71,000 and 9.3% blasts and normal LFT. She received multiple PRBCs and platelets transfusions. CT scan of abdomen showed a 6.4 × 5.5 cm mass within the

gastric antrum. Upper gastrointestinal endoscopy revealed a submucosal, non-circumferential mass partially occluding the gastric antrum (Fig. 1). Histopathological and immunochemical staining of biopsies showed an atypical cellular infiltrate that expressed CD43, lysozyme, myeloperoxidase and positive Leder stain (chloroacetate esterase) (Fig. 2). Repeat bone marrow biopsy was consistent with AML.

**Discussion:** GS commonly involves periosteum/bone, soft tissue, lymph nodes and skin. Gastrointestinal tract is rarely involved with small intestine as the more common site than stomach. Acute GI bleed as in our case, has been reported as the most common presentation. Endoscopically gastric GS have appearance of superficial ulceration, hemorrhagic rugal folds, multiple small nodules and more commonly as a polypoidal mass. Diagnosis is based on tissue biopsy, immunochemical and Leder's staining. Management involves chemotherapy, local radiation or surgical intervention.

**Conclusion:** It's prudent to endoscopically screen patients for gastrointestinal involvement from myeloproliferative or leukemic disorder in the presence of GI symptoms.[figure1][figure2]



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#### **Cronkhite-Canada Syndrome Presenting as Acute Colitis; Confirmed by Colonoscopy, Upper Endoscopy, Capsule Endoscopy, and Pathology**

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Cronkhite-Canada syndrome is a rare disease first described in 1955. The clinical features include diarrhea, nail dystrophy, alopecia, and hyperpigmentation of the skin. We describe a case of Cronkhite-Canada Syndrome presenting as acute colitis with evidence of disease found on upper endoscopy, sigmoidoscopy, and capsule endoscopy.

A 49 year old male presented to the Emory University GI clinic with total body hair loss and bloody diarrhea which began suddenly six weeks prior to presentation. He described the diarrhea as loose, predominantly liquid stool

with red blood mixed in occurring 4–5 times per day. The diarrhea also occurs at night and wakes the patient from sleep. He was seen by a gastroenterologist who performed a colonoscopy and was found to have erythema throughout his colon. He was diagnosed with indeterminate colitis from a biopsy showing mucin filled crypts and chronic active inflammation without malignancy and started on 5-ASA therapy without improvement. At the time of presentation to our clinic, he had no remaining hair on his head and had also lost his eyelashes and body hair including his pubic hair. He also reported that he had lost his finger nails and toe nails. In addition he had a fifty pound weight loss and systemic fatigue. He also reported alterations in his sense of smell and a decreased appetite because food no longer tasted good. Physical exam was notable for diffuse hair loss including loss of his eyelashes, loss of his finger nails and toe nails but was otherwise unremarkable. Upper endoscopy and flexible sigmoidoscopy were repeated in addition to capsule endoscopy for additional evaluation. The upper endoscopy was remarkable for nodular, friable, erythematous gastric mucosa. There was also duodenitis with erythema and ulcerations noted. The esophageal mucosa was normal. The flexible sigmoidoscopy demonstrated erythematous and friable mucosa from the rectum to the transverse colon with exudative ulcerations. Capsule endoscopy showed diffuse, nodular erythematous mucosa throughout the entire small bowel. After a thorough review of the patient's history, physical exam and discussion with our pathologist the diagnosis of Cronkhite-Canada Syndrome was made and treatment was started. The patient was treated with antihistamines, H-2 blockers, prednisone, and the first reported use of the antibiotic Rifaximin for the treatment of Cronkhite-Canada Syndrome with a good response.

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#### **Agenesis of the Gallbladder: A Preoperative Diagnosis Using 4 Imaging Modalities**

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Agenesis of the gallbladder is a rare biliary congenital anomaly, with an incidence rate of 0.01–0.06%. Awareness of this entity by clinicians and radiologists is essential because approximately 23% of affected individuals present with biliary symptoms, including 90% with right upper quadrant pain, 60% with nausea and vomiting, and 35% with jaundice. Agenesis of the gallbladder will frequently be misinterpreted as cholecystitis with cystic duct obstruction, therefore subjecting these patients to undergo unnecessary surgical procedures. We present a case of a 35-year-old female with right upper quadrant pain, nausea, and vomiting, but no jaundice, pruritis, or fever. Physical examination revealed right upper quadrant tenderness with voluntary guarding but without rebound tenderness or Murphy's sign. There were no surgical scars on the abdomen or back. Pertinent laboratory values included a white blood cell count of 4,600 /mm<sup>3</sup>, albumin 4.2, alkaline phosphatase 163, total bilirubin 0.6, direct bilirubin 0.2, AST 98, ALT 93, and GGTP 627. A HIDA scan suggested the diagnosis of acute cholecystitis; however, the gallbladder could not be visualized on ultrasonography or computed tomography of the abdomen. An MRCP was then performed which also failed to visualize the gallbladder but noted an otherwise normal biliary tree, confirming the diagnosis of agenesis of the gallbladder. Even though agenesis of the gallbladder is rare, it should be considered preoperatively in a patient presenting with symptoms of cholecystitis to avoid unnecessary surgery.

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#### **Dramatic Decrease of Gastrin Levels after Extirpation of Metastatic Gastrinoma Lymph Nodes in a Patient with Multicentric Carcinoid and MEN 1**

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Health Care System, Brooklyn, NY and SUNY Downstate Medical Center, Brooklyn, NY.

**Case Report:** A 57-year old male presented with epigastric pain and heartburn. He had two loose bowel movements daily; no weight loss. He had a history of Zollinger Ellison syndrome (ZES) with multiple endocrine neoplasia-1 (MEN-1); medical records indicated that he had undergone a partial parathyroidectomy for hypercalcemia and recurrent renal stones in 1985; in 1992, he was found to have multiple gastric ulcers and a gastrin of 2000 pg/ml; he underwent resection of two duodenal gastrinomas in 1993. He was treated with high dose omeprazole since.

We performed EGD, which revealed over 100 gastric polyps in the stomach, 0.5-cm to 2.5-cm in diameter, and approximately 20 polyps in the first and second portion of duodenum; Gastric pH was 8 on high dose omeprazole. Pathology and immunopathology were consistent with carcinoid tumor. Gastrin level was 21,712 pg/ml.

Abdominal CT demonstrated an enhancing lesion in the tail of the pancreas and multiple enhancing nodules between the pancreas and second and third portion of duodenum; the gastric wall had a thickened, enhancing nodular appearance. Octreotide scan showed uptake in the stomach and duodenum. Gastrin level prior to surgery was 24,332 pg/ml. He underwent resection of peripancreatic, periduodenal, and perigastric lymph nodes and enucleation of the pancreatic lesion. Multiple carcinoid lesions were noted in the stomach and duodenum. No liver metastases were detected. Pathology and immunopathology were consistent with gastrinoma. 1-week later, gastrin level was 8.897 pg/ml. He was started on Octreotide daily, and is now maintained on monthly IM injections. Five months post-op, EGD revealed slight regression of gastric and duodenal nodules; gastrin was 2,359 pg/ml.

**Conclusion:** Gastric carcinoid tumors occur in 15 to 50% of patients with MEN-1 and ZES, and are usually benign. Gastric carcinoids in patients with longstanding MEN-1/ZES may become symptomatic, aggressive, and metastasize to the liver. Surgical excision of gastrinomas in patients with ZES decreases the incidence of hepatic metastases, however long-term biochemical cure is achieved in fewer than 30% of cases. Our patient successfully underwent lymphadenectomy and enucleation of remaining gastrinomas followed by Octreotide therapy with dramatic reduction in his gastrin level as well as symptomatic improvement and regression of his carcinoids.

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### Ischemic Duodenal Ulceration in a Sickle Cell Patient with Sickle Cell Crisis

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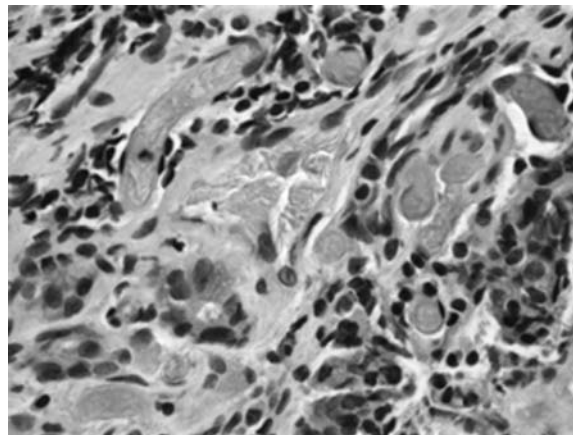
**Introduction:** Sickle cell disease (SCD) is caused by molecular abnormalities in the formation of hemoglobin causing pain crisis from vascular occlusion by sickling. Impaired flow in the microvasculature can lead to ischemia, infarction, and ulceration. We present a case of sickle cell crisis (SCC) causing a duodenal ischemic ulcer.

**Case Report:** A 35 year old woman with SCD presented in SCC with abdominal pain (atypical symptom for her). She began narcotics, fluids, O<sub>2</sub>, and DVT prophylaxis, but her abdominal pain continued. She had 3 episodes of hematemesis. Hgb dropped from 12.9 to 9.8 and she denied NSAID use. She started on a PPI, got 2 units of RBC's, and DVT prophylaxis was stopped, despite risk factors for DVT (cigarette smoking and OCP use). EGD showed hemorrhagic duodenitis and 1 cm ulcer in the bulb (Fig. 1). Ulcer biopsy revealed mucosal capillaries with sickled RBC's and no H. pylori. On day 4, her O<sub>2</sub> saturation dropped from 97% to 89%. CT of the chest showed bilateral PE, she became hemodynamically unstable, and died of cardiac arrest.

**Discussion:** Abdominal pain is common in SCD, with etiologies from splenic sequestration to hepatobiliary disease. With epigastric pain, ischemic ulcer of the duodenum is possible. Ischemic ulcers in SCD are due to primary mucosal infarctions caused by sickling. At low O<sub>2</sub> tension, hgb S tends to

polymerize, causing a distorted RBC with poor deformability leading to arteriolar occlusions causing poor healing of infarcted areas.

**Conclusion:** Complications of ischemic ulcers of the GI tract due to SCD must be in the differential diagnosis of abdominal pain in SC patients. Urgent endoscopic and surgical intervention need to be considered, as PPI's do not heal this ulcer. Use of anti-coagulants needs to be balanced between the risks of PE and increased GI bleed; aggressive endoscopic hemostatic treatment of the ischemic ulcer may be warranted.[figure1]



## 714

### Ascites Still a Dilemma!

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**Introduction:** Ascites is a common finding in clinical practice. It is typically due to liver disease. The etiologic approach of ascites is relatively easy but patients with a mixed picture can sometime complicate the workup.

**Case Report:** Our patient is a 34-year-old previously healthy non-alcoholic Portuguese man who was admitted to Trinitas Hospital on 12/02/2006 complaining of abdominal distension, epigastric pain and significant weight loss. Patient denied any history of illicit drug use, blood transfusion or TB exposure. Physical examination revealed massive ascites with tender abdomen, no jaundice. Preliminary studies included LFTs, INR, amylase, lipase, UA WNL, Hepatitis B, C, HIV, ANA and RF negative. USG and CT abdomen showed massive ascites, normal biliary tree and liver. Paracentesis revealed normal appearing ascitic fluid with SAAG <1.1, wbc 81(Lymph 90%). Gram stain, culture, AFB culture were negative with normal cytology. MRA showed normal portal vein and 2D Echo was WNL. Stool studies did not show any infection or evidence of malabsorption. Peritoneal biopsy was negative for malignancy and tuberculosis. Esophageal, gastric and small bowel biopsies were non-revealing. Patient was treated with multiple paracentesis and empiric antibiotics. Patient improved with resolution of ascites and discharged home.

**Discussion:** Although cirrhosis is the cause of ascites formation in most patients, approximately 15 percent have a cause other than liver disease, including cancer, heart failure, tuberculosis, or nephrotic syndrome. Review of literature revealed that ascites without obvious cause has been associated with dialysis, previous abdominal surgery, hypothyroidism, constrictive pericarditis and mesothelioma. In our case despite extensive workup, it was still a dilemma!

## 715

### Endoscopic Therapy of a Difficult To Treat Pancreatic Duct Stone in a Pediatric Patient

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A 15-year-old male pt with no significant pmh visiting the US from India presented to a PCP for evaluation of acute abdominal pain. He was found to have mid epigastric tenderness and anorexia with frequent episodes of vomiting. The initial work-up revealed elevated serum amylase and lipase levels  $2\times$  above the upper limits of normal. An MRCP was performed which showed a stricture in the pancreatic duct (PD) at the head of the pancreas with a large 3 cm stone within the duct proximal to the stricture. An ERCP was performed (Fig. 1) which revealed similar findings as the MRCP with a dilated PD. A pancreatic sphincterotomy was performed, and the PD stricture was dilated to 6 mm using a balloon dilator system. Several attempts were made to perform mechanical lithotripsy and remove the stone with both a balloon and basket. These attempts were unsuccessful, and a pancreatic stent was placed extending distal to the stone. The patient underwent extracorporeal shock wave lithotripsy (ESWL) after which a repeat ERCP was performed. The stricture was dilated to 6 mm. The remaining stone and many stone fragments were successfully removed during the procedure (Fig. 2). The pancreatic duct was irrigated with saline, and clear effluent was accomplished. Two large caliber stents were placed during the procedure to modify



the anticipated course of pancreatitis. After the procedure, the patient was pain free with amylase and lipase levels now within the normal range. This vignette is an example of successful endoscopic therapy of a difficult to treat pancreatic stone. An alternate treatment strategy considered during the initial consultation included surgical management of the stone by pancreatico-jejunostomy. This more invasive procedure and its related morbidities was avoided by utilizing a combination of ESWL and ERCP.[figure1][figure2]

## 716

### **Segmental Arterial Mediolytic: An Unusual Cause of Ischemic Colitis**

*Robert E. Kraichely, MD, Amy S. Oxentenko, MD\*. Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN.*

**Case:** A 25-year old female presented with acute severe abdominal pain that awoke her from sleep, located in the mid and lower abdomen. It was associated with nausea and diaphoresis. Within hours, she began to have diarrhea, followed by hematochezia, prompting an emergency room visit and hospital admission. Examination revealed no fever, normal bowel sounds, abdominal tenderness without peritoneal signs, and gross blood on rectal exam. CBC, electrolytes, liver chemistries, pancreatic enzymes,  $\beta$ -hCG, and cultures were within normal limits. Colonoscopy revealed erythema and ulcerations around the splenic flexure, with biopsies consistent with ischemic colitis. She received supportive care and symptoms resolved. Upon outpatient consultation, her past medical history was unremarkable. Her only medication was an oral contraceptive. She denied smoking, and had no personal or family history of hypercoagulable conditions. She was tested for hypercoagulable disorders, with none found. Because of her age and absence of an obvious etiology, a CT angiogram was performed which demonstrated focal dissection of the superior mesenteric artery adjacent to the origin of the middle colic and pancreaticoduodenal arteries, with the origin of the middle colic artery narrowed. These findings were consistent with segmental arterial mediolysis as a cause of her ischemic colitis. There was no extension of the dissection or further blood flow compromise upon repeat CT. There was no evidence for a connective tissue or collagen vascular disease. She was placed on beta-blocker therapy and had her oral contraceptive discontinued. Plans were made for follow-up imaging in six months.

**Discussion:** Segmental arterial mediolysis (SAM) is a rare, nonarteriosclerotic, noninflammatory vascular condition characterized by vacuolar degeneration with lysis of the outer tunica media vasorum of the arterial wall. SAM predominately involves the abdominal visceral arteries, although renal, cerebral and coronary arteries can also be affected. Incidence is unknown. SAM can lead to aneurysms, dissection, thrombosis or rupture of the splanchnic and renal arteries. Hemorrhage and shock are most commonly reported, and bowel ischemia or infarction is less frequent. The natural course of SAM is not known, although some speculate it may be a precursor to fibromuscular dysplasia. This case demonstrates that SAM can manifest at a young age, and should be in the differential diagnosis of the patient presenting with bowel ischemia without other known risk factors.

## 717

### **Chronic Diarrhea, Alopecia Totalis and Muscle Cramps in a 36 Year Old Female**

*Samar Harris, MBBS, Kathrin Czarnecki, MD, Harris V.K. Naina, MBBS\*. Internal Medicine, Mayo Clinic, College of Medicine, Rochester, MN.*

To report a case of Satoyoshi syndrome occurring in a Caucasian female. A 36-year-old Caucasian female developed painful muscle cramps of both lower extremities along with bilateral hip pain since the age of 9 years. She was later found to have bilateral femoral head deformities. She attained menarche at the age of 14 years along with development of secondary sexual characteristics. At the age of 16, her symptoms were further complicated with diffuse hair loss in her scalp, axilla and pubic regions.

She became pregnant at the age of 26, and there was complete resolution of her symptoms including reversal of her hair loss. Shortly after an uneventful pregnancy and vaginal delivery of a term baby, her symptoms returned with progressively increasing severity. Two years prior to presentation she developed intermittent self limiting episodic watery diarrhea with each episode lasting for 1 to 2 weeks. There was no associated abdominal pain, nausea, vomiting, or fever. However she did note a 20 pound weight loss.

A clinical diagnosis of Satoyoshi syndrome was made in 2006, and she was started on treatment with prednisone. Her diarrhea and muscle cramps got better. A subsequent EGD and colonoscopy were unremarkable. Mucosal biopsies from small bowel were negative for celiac disease. The biopsies from the colon showed mild chronic colitis.

Satoyoshi syndrome is a very rare systemic autoimmune disease involving the nervous, endocrine, and gastrointestinal systems. The majority of patients with Satoyoshi syndrome has been reported from Japan. Rarely has it been reported in Caucasians. A recent study has shown a common antibody against brain, stomach, and duodenal tissue, in the sera of two patients with this syndrome. GAD antibodies in Satoyoshi syndrome has been reported, but it was negative in our patient. She had symptomatic and clinical improvement with steroids but her alopecia totalis did not resolve completely.

Satoyoshi syndrome should be considered as a differential diagnosis in patients with neurological symptoms and chronic diarrhea with alopecia. These patients would benefit from immunosuppressants.

## 718

**Tanned Lady with Skin Lesions and Liver Disease**

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We illustrate a case of porphyria cutanea tarda manifested as a result of heterozygous hemochromatosis gene mutation.

46 year old female presented with increasing pigmentation of face and blisters on bilateral hands and feet. She had no past medical history, substance abuse and was on no medications. Physical examination showed hyperpigmentation/hypertrichosis of the face, bullous lesions on the dorsal surfaces of hands and feet and accompanied by crusted erosions, atrophic scars, abdominal distension, with positive shifting dullness and bilateral lower extremity edema.

**Evaluation:** Skin biopsy of the bullous lesions revealed Sub epidermal Blister. Urine Wood lamp examination yielded pink fluorescence. Plasma porphyrin level was elevated with fluorescence emission maximum at neutral pH near 619 nm. Urine porphyrin level was elevated. Urine uroporphobilinogen, delta aminolevulinic acid were normal. Fecal porphyrin levels were elevated. Hepatic panel showed elevated ALP, ALT, AST, Right upper quadrant ultrasound showed findings of cirrhosis. Hepatitis serologies and ANA were negative. Ferritin and serum iron level was elevated with normal TIBC. Liver biopsy revealed Iron Overload with severe Fibrosis. Genetic studies for hemochromatosis showed heterozygous H63D mutation.

**Conclusion:** Diagnosis of Porphyria cutanea Tarda was made. Heterozygous H63D mutation being the inciting factor for iron overload. PCT results from deficiency of the uroporphyrinogen decarboxylase in heme biosynthetic pathway. Exposure to hepatotoxins that result in hepatic iron overload is one of the major mechanism. HFE mutations and hepatitis C virus infection are important causes.

Porphyria cutanea tarda should always mandate workup for underlying hepatic iron overload. Mutation analysis for hemochromatosis and liver biopsy may be necessary. Heterozygous hemochromatosis gene mutations, although rare could manifest as iron overload syndromes.

## 719

**Recurrent Colonic Abscesses: A Rare Presentation of Colonic Cancer**

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Colorectal cancer rarely manifests as colonic abscess. Here we have a patient who presented with recurrent colonic abscesses and was diagnosed with adenocarcinoma of the cecum. The literature review did not show any other documented case of colorectal cancer presenting as recurrent colonic abscesses.

A 67 years old African American female with hypertension, anemia, and uterine fibroids was admitted with right lower quadrant abdominal pain for one week. The pain was associated with dark brown watery diarrhea, nausea but no fever, chills or vomiting. She had right lower quadrant tenderness with no rebound or rigidity. Fecal occult blood test was negative.

Two months prior to admission, patient had similar pain and CT scan abdomen revealed right lower quadrant abscess measuring 7.4 cm × 6.8 cm. She underwent CT guided drainage with indwelling catheter for six weeks. Cultures showed enterococcus fecalis and beta hemolytic streptococcus. Antibiotics given. After indwelling catheter removal, patient had recurrent right lower quadrant pain, repeat CT scan abdomen revealed recurrent colonic abscess measuring approximately 6.1 cm × 7.8 cm and repeat CT guided drainage of right lower quadrant abscess was done. Culture showed Aeromonas hydrophilis and Streptococcus viridans. Patient was discharged on antibiotics. Colonoscopy revealed large friable mass in cecum and a small polyp in proximal transverse colon. Cecal mass biopsy showed moderately differentiated adenocarcinoma, and transverse colon biopsy showed tubular adenoma. Right hemicolectomy was performed, and its biopsy showed stage 2, moderately differentiated invasive adenocarcinoma, located in cecum centered on appendiceal orifice extending into the pericolic fat forming a 4 cm mass. Obstruction of appendiceal orifice was seen due to the tumor extension causing dilatation of distal appendix with mucinous dissection of its muscle layer and perforation of mid portion of appendix forming a fistula tract into retrocecal region. Pericolic lymph nodes were negative for metastasis. CEA level was 1.8 prior to surgery and repeat CEA level after surgery was 1.2. Six months post operatively, a surveillance colonoscopy was normal.

Colorectal carcinoma is common in the USA. Its presentation varies therefore, it is a diagnostic challenge for. Above we have reported colonic carcinoma presenting as recurrent colonic abscess. Our patient had normal colonoscopy two years ago.

Recurrent colonic abscesses can be an indicator of an occult colorectal carcinoma.

## 720

**VIPoma – A Case of Abrupt Onset Diarrhea in an Elderly Patient**

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An 85 year old previously healthy Caucasian female presented with a 2 month history of a sudden onset diarrhea involving 7–10 large, watery, non-bloody bowel movements per day. The diarrhea was unaffected by fasting, and she denied any abdominal pain, fevers, sick contacts, or recent travel. Physical exam was significant for orthostasis. Laboratory data demonstrated hypokalemia and a non-anion gap metabolic acidosis. Common infectious etiologies were initially ruled out with negative fecal leukocytes, stool gram stain and culture, Clostridium difficile toxin, ova and parasites, and Giardia studies. A colonoscopy was unremarkable, and an EGD revealed no evidence of celiac sprue. Stool electrolytes revealed a low stool osmotic gap suggesting a secretory diarrhea. Subsequent studies for gastrin and 5-HIAA were normal, and the patient denied any laxative use. However, a VIP level was found to be elevated at 359. A subsequent CT and MRI showed no masses or evidence of metastasis. An iodine 123 meta-iodobenzylguanidine (I-123 MIBG) scan ultimately indicated an area of increase uptake in the fourth part of the duodenum. The patient refused surgical intervention, and she was placed on octreotide injections, which significantly improved her diarrhea. A follow-up VIP level showed a decrease to 28.

VIPomas are extremely rare neuroendocrine tumors with an incidence of 1:10,000,000 per year. The hypersecretion of vasoactive intestinal peptide results in the Verner-Morrison or WDHA syndrome, which includes large

volume watery diarrhea, hypokalemia, and achlorhydria. VIPomas are typically found in adults 30–50 years of age and have a gradual onset of symptoms. The majority of these tumors are located in the tail of the pancreas and are often metastatic at the time of diagnosis. Treatment usually involves octreotide to inhibit hormonal secretion. This particular case represents an uncommon presentation as the patient was considerably beyond the normal age range and presented with a sudden rather than gradual onset of symptoms. In addition, the tumor was ultimately located in the duodenum. Although neuroendocrine tumors such as VIPomas are an exceedingly rare cause of diarrhea especially in the elderly, they should be considered as a potential etiology in any secretory diarrhea.

## 721

**Idiopathic Hepatic Angiosarcoma**

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A 47 year old white male was referred to evaluate rapidly progressing liver disease. The patient complained of 6 months duration of dull, constant, mid-epigastric abdominal pain with radiation to the back. The onset was gradual with a persistent progression in severity requiring escalating doses of acetaminophen and naproxen. Other symptoms included anorexia, weight loss, and nausea. Exam revealed a middle aged man with a sallow complexion. He had signs of temporal wasting, palmer erythema and spider angiomas. His liver span was 10 cm with a firm smooth edge. He had mild abdominal distention without focal tenderness and a positive fluid wave.

Laboratory data revealed non-specific abnormalities in his liver function tests. CT scan of his abdomen demonstrated a nodular liver with several small enhancing nodules. A non-contrast CT scan ten months prior revealed a normal appearing liver. Extensive serological work up was negative. Tumor markers were within normal limits. MRI had diffuse signal abnormalities including a 2.5 cm area near the dome of the right lobe of the liver. Biopsy of the right dome mass came back as nondiagnostic soft tissue and blood clot. A random liver biopsy was noted for sinusoidal dilation without evidence for fibrosis. Repeat MRI two months after the biopsy showed an additional 4 cm infiltrating mass straddling the hepatic vein. The paracentesis showed thick, vibrant green ascites with negative cytology. The hepatic gradient pressure was increased. Transjugular biopsy revealed acute centrilobular necrosis, severe sinusoidal dilation, and a single area of atypical hepatocellular regeneration. Due to diagnostic uncertainty a laparoscopy with ultrasound guided liver biopsy was performed. The liver grossly appeared cirrhotic. There were nodules seeding the peritoneal wall as well as a posterior wall bladder mass. Biopsies confirmed the diagnosis to be a high grade metastatic epitheloid hepatic angiosarcoma.

Hepatic angiosarcoma is a rare malignant vascular tumor. The diagnosis can be difficult due to the rarity of the tumor. This tumor mimics more common disorders and lacks pathognomonic signs. The finding of a thick, vibrant green ascites had not been reported before. Open biopsy is often needed to make the diagnosis. The clinical course is aggressive and there are minimal treatment options available.

## 722

**Dissection of an Unusual Gastric Mass Using Rat-Tooth Forceps**

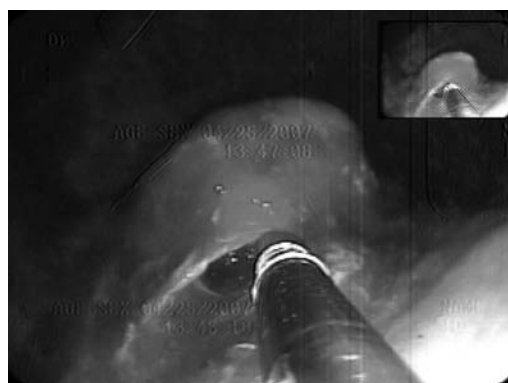
Patrick J. McDevitt, DO, Arnab Biswas, DO, Abraham Mathew, MD\*. *Department of Internal Medicine, The Penn State Hershey Medical Center, Hershey, PA and Department of Gastroenterology and Hepatology, The Penn State Hershey Medical Center, Hershey, PA.*

A 71 yr old Asian male with a history of renal cell carcinoma is referred for EUS evaluation of a 3 cm mass located in the gastric cardia. Biopsies at previous EGD were negative for evidence of neoplasm. EUS was performed with a radial and linear scope. The lesion was confined to the submucosa separate from the muscularia propria. The complex lesion was 22 mm ×

20 mm with anechoic and hypoechoic regions. FNA and tunneled biopsies were negative. Endoscopic resection was performed given the documented ultrasonographic properties. Saline was injected circumferentially adjacent to the lesion. Needle-knife was used to incise three-quarters around the base. Rat-toothed forceps were then used to enter the submucosal plane. Dissection was accomplished by opening and closing movement of the forceps. The endoscope was retroflexed to repeat this sequence on the distal aspect until the lesion was completely elevated. Using standard snare polypectomy technique, the nearly excised mass was detached from the gastric wall. Minor bleeding was controlled with epinephrine injection and hemostatic clips. The pathology report showed the lesion to be a buried inverted fundic gland polyp.

Submucosal masses are a frequent finding at endoscopy. Common submucosal lesions include leiomyomas, leiomyosarcomas, lipomas, stromal tumors, carcinoid tumor, granular cell tumors, duplication cysts or varices. While fundic gland polyps are a common finding, inverted polyps are a rare occurrence.

Endoscopic mucosal resection (EMR) has been used for the removal of intramucosal neoplasms of the gastrointestinal tract with success. This procedure relies on the snare technique and has been limited to lesions less than 20 mm. Endoscopic submucosal dissection (ESD) is a newer technique developed to overcome the limits of EMR. The snare technique is not used for ESD and this procedure relies on a needle knife for en bloc resection. We present a unique approach for the removal of a submucosal lesion found to be an uncharacteristic fundic gland polyp.[figure1]



## 723

**Hepatic Adenomatosis: A Rare Clinical Entity with Unique Characteristics**

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**Introduction:** Hepatic adenomatosis (HA) is a rare entity. Complications can ensue and may be related to hemorrhage, excessive growth with pain and malignancy. We present a case in a 33-year old female suffering from persistent growth of HA despite past surgical intervention.

**Case:** Caucasian female presents with right upper quadrant tenderness (RUQ), nausea, and vomiting worsening over three days. Past history significant for a right lobectomy and left lateral segmentectomy of the liver after a fall 20 years earlier. The patient used oral contraceptives for less than a year as a teenager. On exam, she was tachycardic and hypotensive. Abdomen was distended, firm, RUQ tenderness, and hepatomegaly. Bowel sounds were present. Laboratory data revealed H&H 12/36, AST 216 U/L, ALT 216 U/L, albumin 3.8 g/dl, alkaline phosphatase 138 U/L, INR 1.1, AFP 1.5 ng/mL, and lactic acid 2.9 mmol/L. Initial CT scan demonstrated extravasation of contrast in the caudate lobe suggestive of a bleed. Angiogram showed an



irregular branch of the hepatic artery to the caudate lobe which was embolized. Repeat CAT scan revealed multiple hepatic lesions and hemorrhage (subcapsular, retroperitoneal, and intraperitoneal). Her condition worsened thus she was listed and received a cadaveric liver transplant. The explanted liver showed presence of a 17×10×5 cm hematoma in the liver. It also contained 50–100 adenomas ranging in size from 0.5 cm–4.5 cm. Pathology revealed hepatic adenomatosis.

**Discussion:** Hepatic adenomatosis is a rare entity characterized by greater than 10 adenomas. Unlike solitary hepatic adenoma, there is lack of female predominance or association with glycogen storage diseases. Lesions do not have a tendency towards influence by steroid or estrogen use. The etiology is poorly understood and is associated with congenital or acquired abnormalities of hepatic vasculature.

Clinically, these lesions are more painful and result in significant hepatomegaly. Bleeding and malignant transformation occurs in 62% and 13% of cases respectively. Due to the risk of hemorrhage and malignancy, resection of the largest and most vulnerable lesion is often required. Surgical resection has been shown to decrease abdominal pain and lead to longer hemorrhage free intervals and need close surveillance. Patients who progress despite radiological and surgical interventions require liver transplantation.

## 724

### Obstructive Jaundice Secondary to a Pancreatic Plasmacytoma

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**Case Report:** A 37 year old male recently diagnosed with multiple myeloma and on therapy with thalidomide presented with epigastric pain and jaundice. At the time of presentation, the pertinent positives on physical exam were jaundice and a mildly distended abdomen with epigastric tenderness. Total bilirubin was 4.2 mg/dL with direct fraction 3.3 mg/dL, alkaline phosphatase 250 U/L, AST 107 U/L, and ALT 160 U/L. Other blood tests including tumor markers were normal. A CT scan of the abdomen revealed a large pancreatic mass measuring approximately 8 cm × 8 cm encasing the celiac axis and abutting the superior mesenteric artery. Endoscopic ultrasound demonstrated a heterogeneous and diffusely hypoechoic mass replacing the head, uncinate process, neck, and proximal portion of the body of the pancreas. In the mid body of the pancreas there was a demarcation between the infiltrating tumor and the distal pancreas. The common bile duct could not be identified in the head of the pancreas. FNA of the mass revealed hemorrhagic smears containing sheets of plasma blasts and cells consistent with myeloma. The patient was diagnosed with pancreatic plasmacytoma in the setting of multiple myeloma. Treatment was initiated with bortezomib. By the third cycle, symptoms had improved and hepatic blood tests had normalized.

**Discussion:** Extramedullary myeloma is rare and most commonly manifests in tissues rich in reticuloendothelial cells such as those found in the head, neck, and upper respiratory tract. Gastrointestinal involvement has been reported in approximately 10% of cases and usually involves the liver or spleen. The pancreas is only rarely involved and the diagnosis is often made postmortem with an incidence rate of 2.3% based on autopsy studies. Obstructive jaundice and abdominal pain are the most common symptoms characterizing myeloma of the pancreas.

Previous case reports of pancreatic plasmacytoma have described laparotomy as the method of choice in obtaining a tissue diagnosis. This case highlights the utility of EUS as a surgery-sparing diagnostic modality in a patient with a large pancreatic mass. We also are reminded that pancreatic plasmacytoma should be considered in the differential diagnosis of a heterogeneous pancreatic mass, especially in the setting of multiple myeloma.

## 725

### Ischemic Colitis Masquerading as Crohn's Colitis in a Patient with Protein C Deficiency

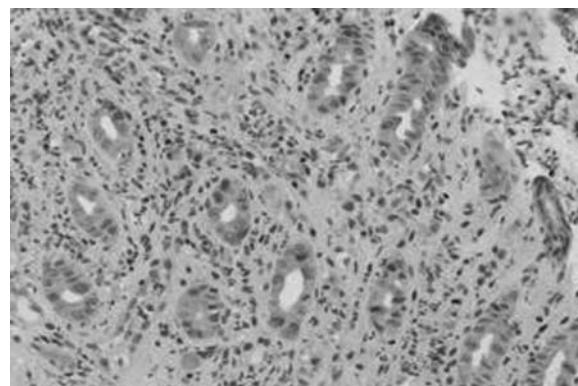
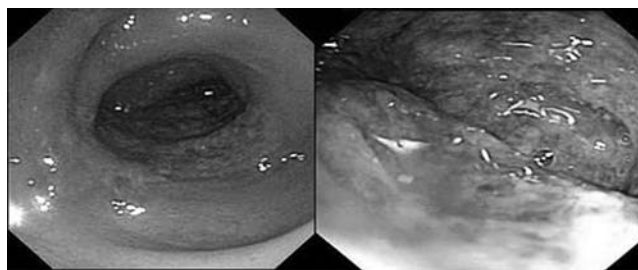
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**Introduction:** Acute mesenteric ischemia from mesenteric vein thrombosis [MVT] is a rare manifestation of a hypercoagulable state like protein-C/S deficiency. We report a case of protein-C deficiency with ischemic colitis mimicking the radiological and endoscopic features of Crohn's colitis.

**Case Description:** 29 yr/F with protein-C deficiency with no prior complications presented with abdominal pain, tenesmus and bright red blood per rectum. She denied fever or any constitutional symptoms. CBC, liver function tests and coagulation profile were normal. CT scan of the abdomen/pelvis with contrast showed diffuse thickening from mid-transverse colon to the rectum and ruled out MVT. Stool studies including bacterial cultures, clostridium difficile toxin were all negative. Sigmoidoscopy showed skipped areas of bleeding ulcerated mucosa with inflammatory changes in the recto-sigmoid colon suggesting Crohn's colitis and the patient was started on mesalamine [Fig. 1]. Rectosigmoid biopsy showed ulceration, coagulative necrosis and inflammation with fibrin thrombi consistent with ischemic colitis secondary to MVT [Fig. 2]. There was no evidence of chronic changes to suggest inflammatory bowel disease.

**Discussion:** MVT should be suspected when acute abdomen develops in patients with prior thrombotic episodes or a documented thrombophilic state. It was postulated that in our patient protein-C deficiency led to MVT which was not revealed on the CT scan and the bleeding was secondary to mesenteric ischemia. CT scan is considered the diagnostic test of choice and anticoagulation is the standard of care. High index of clinical suspicion, early diagnosis and treatment can prevent progression to gangrenous bowel.

**Conclusion:** Our case underscores the association of mesenteric vein thrombosis with prothrombotic disorders and brings to attention that it can be missed on imaging studies.[figure1][figure2]



## 726

### GI Classification Systems: Spanning the Globe

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Gastroenterology is replete with classification systems and criteria. These systems have sometimes been named for the cities in which they were created to facilitate easy recall by clinicians. To our knowledge, a report of classifications based on place of origin has never been published. A Medline search was conducted to identify geographically named classification systems. Twenty-one such classifications/criteria were identified.

We present the criteria/classifications listed below in the format of a world map, all with in-depth descriptions; each system is illustrated on the map corresponding to the place where it was first published.

#### Esophagus

- Seattle Protocol for Barrett's Esophagus
- LA Classification for Esophagitis
- North Italian Endoscopic Club for the Study and Treatment of Esophageal Varices

#### Stomach

- Sydney Classification for Gastritis
- Glasgow Dyspepsia Severity Score

#### Colon

- Bethesda Criteria for Testing Colorectal Tumors for Microsatellite Instability
- Amsterdam Criteria for HNPCC
- Paris Classification for neoplasia of the GI mucosa

#### Liver

- Milan Criteria for Liver Transplantation for Hepatocellular Carcinoma
- Barcelona Criteria for Liver Transplantation for Hepatocellular Carcinoma
- UCSF Criteria for Liver Transplantation for Hepatocellular Carcinoma
- Pittsburgh Criteria for Liver Transplantation for Hepatocellular Carcinoma
- King's College Criteria for acetaminophen-induced and non-acetaminophen induced acute liver failure

#### Biliary

- Mayo Risk Score for Primary Biliary Cirrhosis
- Oslo Risk Score for Primary Biliary Cirrhosis
- Milwaukee Classification for Sphincter of Oddi Dysfunction

#### Pancreas

- Atlanta Criteria for Pancreatitis
- Cambridge Classification for diagnosis of chronic pancreatitis based on ERCP

#### IBD/IBS

- Vienna Classification for Crohn's Disease
- Montreal Classification for Ulcerative Colitis
- Rome Criteria for Irritable Bowel Syndrome

## 727

### A Tale of Two CTs

David J. Cozzi, DO, Robert E. Smith, MD\*. *Gastroenterology, Geisinger Medical Center, Danville, PA.*

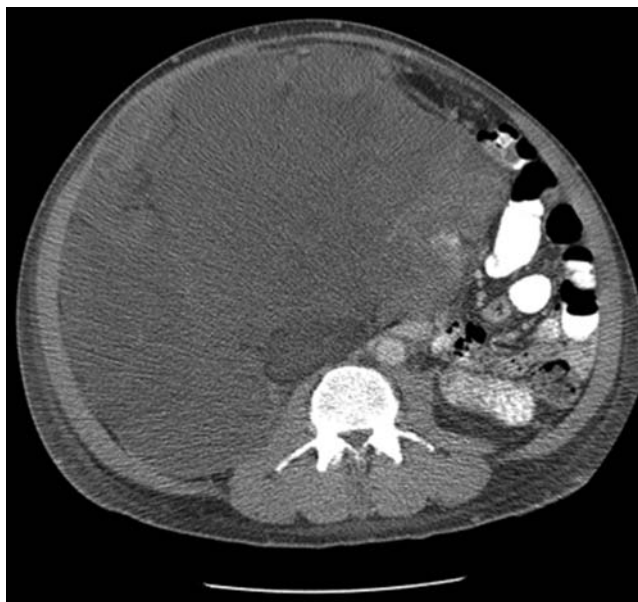
A 52 year old male with no significant past medical history underwent further evaluation of a right retroperitoneal soft tissue mass found on CT measuring 20 cm in its greatest dimension. He had been complaining of right flank discomfort with an associated 15 pound weight loss over the past 6 weeks. Coincidentally, his wife had noted a small lump on the right anterior abdomen that had been progressively enlarging. The patient underwent a CT guided biopsy of the mass that favored a myxoid liposarcoma.

He was arranged for surgery shortly thereafter, however the patient cancelled the procedure and his whereabouts were unknown. Multiple attempts were made to contact the patient, without success. Three months later, the patient re-established contact and underwent a preoperative abdominal CT (Fig. 1). His findings dramatically worsened. His mass extended from the inferior aspect of the liver to the lower pelvis and from the right chest wall to the left mid abdomen. There was evidence of disseminated disease and massive displacement of the internal organs.

He underwent a radical surgical resection, including a right nephrectomy/adrenalectomy, partial right hepatectomy with cholecystectomy and

right hemicolectomy. The excised mass measured 42 × 32 × 20 cm and weighed 11.8 kg. His only post-surgical complication was a perihepatic abscesses that was successfully treated with antibiotics and drainage. A repeat CT was obtained and marked improvement was noted (Fig. 2).

**Discussion:** Liposarcomas are soft tissue sarcomas arising from mesenchymal tissue with its location in the retroperitoneal region accounting for 20% of all sarcomas. Early metastases are uncommon, with the lungs being the most frequent site. This case demonstrates a rapidly growing, disseminated liposarcoma with extraordinary imaging revealing extreme displacement of the internal organs and dramatic postoperative improvement.[figure1][figure2]



## 728

### An Uncommon Occurrence of Intestinal Spirochetosis in an Immunocompetent Host

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**Introduction:** Intestinal spirochetosis (IS) is a condition defined morphologically by the presence of spirochetal microorganisms attached to the apical cell membrane of the colonic and rectal epithelium. It is a rare disease and difficult to diagnose, as its symptoms resemble those seen in many other common diseases. It has an increased prevalence in immunocompromised hosts particularly homosexual men and HIV-infected individuals but few symptomatic cases in immunocompetent hosts have been described. Clinical significance in individual cases has remained unclear. There is still controversy as to treatment with antibiotics (metronidazole or Penicillin G) and eradicating organisms will result in symptomatic improvement.

**Case Report:** We report a case of a 54 year old African American male with a 10 year history of intermittent watery diarrhea. He reported up to 4 bowel movements per day with no associated abdominal pain or cramping. He also reported intermittent hematochezia. Patient's only other medical problem included hypertension. Our patient is a painter and also involved in maintenance work on old roofs and claimed to have frequent contact with excreta from birds and rodents including mice. Physical examination of the patient was unrevealing. An initial laboratory workup that included complete blood count, basic metabolic panel, and liver function tests was normal. Stool cultures were negative; however, the presence of bright red blood and diarrhea prompted a colonoscopy which showed a normal appearing colonic mucosa throughout and moderate sized internal haemorrhoids. Random colon biopsies were obtained to evaluate for microscopic colitis which revealed the presence of spirochetes on the surface of colonic epithelium which were confirmed by positive staining with Dieterle stain. The patient was treated with metronidazole 500 mg 3 times per day for 14 days, and showed improvement.

Intestinal spirochetosis should be included in the differential diagnosis of chronic diarrhea not only in immunocompromised but also in immunocompetent patients. A colonoscopy with biopsy will aid in the diagnosis of this disorder. Treatment with metronidazole or penicillin G should be considered in symptomatic patients with intestinal spirochetosis.

## 729

#### Successful Endoscopic Dilation of Cervical Esophageal Webs: Two Case Reports

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Esophageal rings and webs are the most common structural abnormalities in the esophagus. We present two elderly females with dysphagia and significant weight loss secondary to Cervical Esophageal Webs (CEW). Here we review our recent successful experiences with endoscopic controlled and fluoroscopic guided rupture of these webs.

Two females at the ages of 76 and 87 presented with a six month period of progressive dysphagia and significant weight loss. A barium swallow study demonstrated a thin area of circumferential narrowing in the cervical esophagus, suggestive of CEW.

Because of the high location of the lesions in these two cases, all of the treatment options including surgical resection of the web were considered. Pneumatic dilatation of the web was performed after endotracheal intubation. During the endoscopy, the esophageal web was visualized and under fluoroscopy a guide wire was passed through the narrowing. The balloon was positioned across the web, dilated to 10-mm and subsequently to 13-mm in diameter. Rupturing of the webs was confirmed by bleeding from the site of the cervical web. The scope was then passed through this area without resistance. Brush cytology and mucosal biopsies were then obtained from the web area, which did not demonstrate any malignant process. Patients were discharged the day after the procedure with no complications. During the six month follow up none of the patients complained of recurrent dysphagia.

The first proposed treatment option for benign structural abnormalities of the esophagus is lifestyle modification, including modifying eating habits. One or multiple attempts of esophageal dilation can be implemented in persistent

cases via pneumatic, Savary, or Maloney dilators. Endoscopic electrosurgical incision or Nd:YAG laser incision of the esophageal rings have also been used in refractory cases. Removal of the ring surgically is rarely necessary for persistent dysphagia.

Our successful management of these patients suggests the need for a close multidisciplinary approach for optimal patient care. We think less invasive interventional treatments like pneumatic dilation can be used initially. Endotracheal intubation should be considered to reduce the risk of aspiration and asphyxiation. In the event of treatment failure or in case of complications, esophagotomy and surgical resection of the web can be considered.

## 730

#### Endophthalmitis Complicating Klebsiella Pneumoniae Liver Abscess: An Infrequently Recognized Complication

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Endogenous endophthalmitis is a well described metastatic complication of pyogenic liver abscess that can lead to devastating ocular complications especially in immunocompromised host. Its diagnosis is often delayed due to the sub-clinical presentation. We report one of the few cases in Western literature of metastatic endophthalmitis in the setting of Klebsiella pneumoniae liver abscess.

A 50 year old South Asian male presented to his primary care physician with 4 days of flu like symptoms and fevers up to 40°C. Initially, he complained of new onset right eye pain, photophobia, and blurred vision. Ophthalmologic evaluation noted hypopyon and iridocyclitis of the right eye. Vitreal tap Gram stain revealed Gram negative bacteria. Laboratory data at that time included a leukocyte count of 12,900 with eighty percent neutrophils; AST 43 and ALT 98. The patient was admitted to the hospital three days after initial presentation for aggressive broad spectrum antibiotic therapy. Suspicion of a gastrointestinal source led to a liver ultrasound that demonstrated multiple abscesses in the right hepatic lobe. Percutaneous drainage returned grossly purulent fluid which yielded Klebsiella pneumoniae upon culture. Despite resolution of his sepsis, his ophthalmologic condition worsened requiring enucleation 20 days after initial presentation.

First described in Taiwan in the early 1990s, hepatic abscess secondary to Klebsiella pneumoniae is now an emerging disease in western countries. Reports in the literature have been steadily increasing, and cases have been described in all races. The virulence of K. pneumoniae is notable, and early detection of this pathogen is essential. Endophthalmitis is the most common metastatic complication of Klebsiella hepatic abscess. Intravenous antibiotics commonly employed to treat hepatic abscesses are often insufficient to treat this grave ocular complication. Successful treatment regimens for Klebsiella endophthalmitis often include intravenous and intravitreal antibiotics as well as early vitrectomy to attempt preservation of visual acuity.

1. K. pneumoniae needs to be recognized as a highly invasive organism causing ocular complications in immunocompetent hosts with pyogenic hepatic abscess
2. Early ophthalmic intervention needs to be emphasized in patients with Klebsiella pneumoniae hepatic abscesses and ocular symptoms to prevent permanent visual impairment.

## 731

#### Schistosoma Mansoni in the Stomach – A Rare Find!

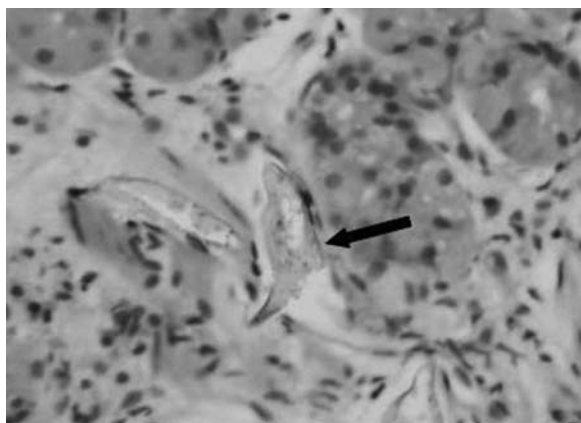
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Schistosomiasis occurs as a result of immune response to the schistosome ova in the tissues of the body. The ova of various schistosomes have been reported in biopsy specimens of rectum, liver, intestine, bladder and rarely

from ectopic sites as bronchial biopsy. We present a very rare case of gastric schistosomiasis caused by *Schistosoma mansoni*.

**Case report:** A 65 year old man, originally from Puerto Rico, who had lived in the US for four decades but travelled frequently to the Caribbean was being followed up for compensated hepatitis C cirrhosis. He underwent elective esophagogastroduodenoscopy to rule out esophageal varices. On EGD, there was no evidence of esophageal or gastric varices or portal gastropathy suggestive of portal hypertension. A small shallow pre-pyloric ulcer was seen and the mucosa in the body of the stomach was noted to have a salt and pepper appearance. Biopsies were obtained and pathology from the body of the stomach revealed several granulomas with *S. mansoni* ova in the lamina propria [Fig. 1]. The patient admitted walking bare foot in water several times over the years in Puerto Rico. He denied having abdominal pain, nausea, vomiting, diarrhea or bleeding. Stool was tested multiple times and did not reveal any ova or parasites. The patient was treated for gastric schistosomiasis with Praziquantel at a dose of 20 mg/kg. Repeat EGD done two months later did not show schistosoma ova in gastric biopsy. The patient was advised to avoid walking bare foot in water in the endemic areas.

**Discussion:** Schistosomiasis can be diagnosed by detecting ova in feces or urine, from various tissues of the body or by serological testing. The ova of different species can be identified by their characteristic appearance. *S. mansoni* ova have a prominent lateral spine. Schistosomiasis is usually asymptomatic as was the case in our patient but intestinal schistosomiasis can present as abdominal pain, diarrhea and iron deficiency anemia. Gastroenterologists should be aware of gastric schistosomiasis as a rare entity that can be successfully treated with Praziquantel.[figure1]



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### Collagenous Colitis Associated with Common Variable Immunodeficiency

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Common Variable Immunodeficiency (CVID), a group of 20–30 heterogeneous disorders, is associated with a broad spectrum of clinical manifestations including gastrointestinal diseases. Common manifestations include nodular lymphoid hyperplasia, inflammatory bowel disease (Crohn's, ulcerative colitis), giardiasis, pernicious anemia, and sprue-like illness. In this report, a rare case of collagenous colitis associated with CVID is described. A patient with an 11 year history of CVID, stable on monthly IV gamma-globulin therapy, presented to the clinic with progressively worsening loose bowel movements over a course of 3 years. Stool culture was negative for ova and parasites, blood and mucus. Upper gastrointestinal endoscopy showed normal appearing esophagus, stomach, duodenum and jejunum as well as a normal colonoscopic appearance. Duodenal biopsies showed no evidence of giardiasis and terminal ileum biopsies were unremarkable. Random colonic

biopsies demonstrated microscopic colitis consistent with collagenous colitis. Immunostaining for CD3 highlighted numerous intramucosal lymphocytes, and trichrome stain revealed a thickened subepithelial collagen band. Collagenous colitis, a rare entity itself, occurs in small percentage of patients who present with chronic diarrhea. The prevalence of CVID is approximately 1 in every 50,000 and to discover this combination is unusual, as there has only been one reported case thus far in the reviewed literature. This report highlights the presentation, diagnostic workup and clinical course in this patient with a rare combination of unusual conditions.

733

### A Challenging and Unusual Presentation of a Case of Acute Pancreatitis

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**Introduction:** The most common causes of acute pancreatitis is from bile stones, alcohol abuse and some uncommon causes being drug-induced, idiopathic, trauma, pancreatic cancer, post-ERCP ischemia, vacuolitis, inflammatory bowel disease. However acute pancreatitis in the setting of uncontrolled rapid atrial fibrillation with systemic embolization should be one of the differential diagnoses to be considered during the work up of Idiopathic pancreatitis.

**Case Presentation:** We report a case of 83 y/o male who presented to the emergency room with abdominal pain radiating to the back. Labs on admission showed elevated amylase and Lipase. Past medical history significant for Atrial Fibrillation. For some medical reasons patient was not on coumadin. Initial CT abdomen did not show any significant pathology in the abdomen. Over the next 24 hrs there was a significant change in the patient's mental status, so we repeated a CT abdomen and CT head which actually showed significant infarcts in the spleen, pancreas and also acute ischemic infarct in the cerebral cortex. This patient probably had Acute pancreatitis secondary to the emboli from rapid atrial fibrillation which is an unusual entity. Though this patient was started on standard anticoagulation, it had to be discontinued as the ischemic infarcts converted to hemorrhagic lesions.

**Discussion:** This was a challenging case because, what was initially thought to be an 'idiopathic' acute pancreatitis turned out to be an ischemic pancreatitis. Our patient had a very deleterious course with a fatal outcome and ended up with ARDS. Management of such cases is a real challenge!

734

### Zenker's Bezoar as a Cause of False-Negative Modified Barium Swallow in a Patient with Dysphagia

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Zenker's diverticulum occurs when abnormally high intra-bolus pressures generated during swallow leads to protrusion of mucosa through an area of anatomic weakness in the pharynx. Patients may experience dysphagia, aspiration, choking, regurgitation, voice changes and weight loss as a result of Zenker's diverticulum.

A 93 year old female was admitted to our hospital for aspiration pneumonia. Modified barium swallow demonstrated oropharyngeal dysphagia with lingual and pharyngeal weakness and retropulsion of the bolus from the esophagus into the pyriform sinuses leading to aspiration. Of note, there was no Zenker's diverticulum identified. These findings made placement of a percutaneous endoscopic gastrostomy tube (PEG) requisite. On upper endoscopy we found a large left-sided Zenker's diverticulum with an impacted bezoar (Zenker's bezoar). The Zenker's bezoar was successfully removed with a Roth Basket (Fig. 1), and the PEG subsequently placed by a push method over a wire to facilitate passage of the tube beyond the Zenker's diverticulum (Fig. 2).

This case demonstrates that a modified barium swallow may fail to demonstrate a Zenker's diverticulum when a Zenker's bezoar is present. The Zenker's bezoar likely contributed to the oropharyngeal component of this patient's dysphagia.

This is only the third reported case of a Zenker's bezoar. This is the first reported case of a Zenker's bezoar leading to a false-negative modified barium swallow. We recommend considering the presence of Zenker's bezoars in debilitated elderly patients who appear to have oropharyngeal dysphagia on modified barium swallows, without prior histories of neuromuscular compromise.[figure1][figure2]



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#### A Rare Case of Hepatotoxicity

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Medications, both prescription and complementary, are increasingly recognized causes of hepatotoxicity. Hepatic injury from drug accounts for approximately 2–5% of hospitalizations for jaundice, and is the most common cause of fulminant hepatic failure in the United States. We present one such case.

A 57 yo man presents to the hospital with a 1 week history of nausea, vomiting, and dark urine. Evaluation in the emergency room revealed AST

239, ALT 497, alkaline phosphatase 231, and total bilirubin of 5.4. He was admitted, and evaluated by the gastroenterology consult service for a possible ERCP. Workup included hepatitis serologies, autoimmune serologies, iron studies, and an abdominal ultrasound. There was no cholelithiasis or biliary dilation, so the case was referred to hepatology.

On further questioning of the patient, he admitted to taking a variety of over-the-counter herbal formulations, and had been taking them for over 2 years. In addition, his primary care physician started atenolol for hypertension within the last month. The patient underwent a liver biopsy to rule out autoimmune hepatitis versus viral hepatitis. The biopsy showed granulomatous hepatitis with an unusual number of eosinophils suggestive of drug induced liver injury. The patient was instructed to stop all herbal medications and the atenolol was changed to amlodipine. Follow-up in clinic revealed that his liver enzymes and bilirubin normalized.

Idiosyncratic drug reactions typically occur within the first 6–12 months after initiation of the medication. In this patient's case, the complementary medications were first on our list of potential culprits. However, he had been taking them for over 2 years which places this group of medications further down the list. The initiation of atenolol for treatment of hypertension, which occurred one month before his presentation to the emergency room, is a more likely suspect, perhaps by interaction with the complementary medications. Antimicrobials and anticonvulsants are the two most common medication groups that cause drug-induced liver injury. However, all clinicians should be cognizant of the fact that any prescribed or complementary drug may cause hepatotoxicity, and a thorough medication history is vital.

736

#### Choledochal Semi Volvulus with Normal LFTs: A Complication of Paraesophageal Hernia, with Literature Review

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86 year old lady presented with sudden onset of sub-sternal and epigastric pain, with radiation to the neck and the back, associated with nausea, palpitation, diaphoresis, and vomiting dark material. **PMH:** Long standing hiatal hernia with bloating, belching, and chest discomfort. BP 220/110. All labs normal except troponin slightly elevated 0.06. **Initial diagnosis:** Acute Coronary Syndrome. Urgent Cardiac catheterization was normal. CT of the abdomen revealed a large paraesophageal hernia with all of the stomach located intra-thoracically, with possible incarceration, along with a hugely distended gallbladder, with dilation of CBD to 13 mm with no gallstones. Patient was taken to OR for reduction and fixation of hernia. An abdominal approach was taken, upon opening of the abdomen a large hemorrhagic, gangrenous gallbladder was seen along with hiatus hernia with pulled choledochal ductal system along with the tenting of duodenum. Intraoperative cholangiogram showed no filling defect or gall stones. Patient underwent cholecystectomy along with reduction and fixation of hiatus hernia.

**Literature Review:** 4 similar cases have been reported.

**Miller and Thompson (1977):** Intermittent dislocation of Liver; A syndrome associated with volvulus of stomach, transverse colon and obstructive jaundice.

**Llaneza PP et al. (1986):** Extrahepatic obstruction of CBD at the diaphragmatic hiatus in association with intrathoracic volvulus. **Lamouliatte et al. (1992):** Biliary obstruction complicating diaphragmatic hiatus hernia with jaundice due to choledochal dislodgement and torsion. **Caldiero et al. (2001):** Choledochal semi volvulus with jaundice due to hiatal hernia. All the 4 cases presented with cholestatic syndrome secondary to either obstruction or stretching of CBD in the diaphragmatic hiatus and hiatus hernia was diagnosed retrospectively. By contrast, our patient presented with chest/ epigastric pain with normal LFTs and was subsequently found to have gangrenous acalculous cholecystitis in association with incarcerated hiatus hernia. This observation emphasizes the possibility of direct relationship of gangrenous cholecystitis and hiatus hernia even with normal LFT, could be due to intermittent stretching or tension of CBD. If time permits HIDA scan is recommended to confirm the diagnosis. But, if the clinical suspicion is

high, an abdominal approach is recommended to repair the volvulus and at the same time explore the gallbladder to reduce the added mortality of these coexisting clinical entities.

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### Metastatic Breast Cancer Mimicking Small Bowel Crohn's Disease

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**Introduction:** Small bowel involvement of metastatic breast cancer is a rare but recognized entity. It can present in a number of ways and can often be confused with primary disorders of the gastrointestinal (GI) tract such as Crohn's disease. We present a case of metastatic breast cancer to the terminal ileum initially presenting as abdominal pain.

**Case:** A 62 year old Caucasian female with metastatic breast cancer to bone presented with left lower quadrant pain for 6 months. The pain was dull without radiation and no aggravating or relieving factors. She complained of no other GI related symptoms such as constipation, diarrhea, nausea, vomiting, weight loss or blood in stool. There was no known family history of colon cancer or inflammatory bowel disease. Initial workup included a CT scan which showed nonspecific wall thickening of the terminal ileum. A small bowel follow through was subsequently done and revealed mucosal effacement and nodularity of the last 15 cm of the terminal ileum. A colonoscopy to the terminal ileum was then done. Endoscopically, the terminal ileum appeared grossly abnormal with several ulcerations and surrounding erythema and edema. The colonic mucosa appeared normal except for scattered diverticulosis. Biopsies of the terminal ileum revealed chronic inflammation.

At that time the patient was suspected to have Crohn's disease but was not treated as she did not follow up with a gastroenterologist. One year later as she remained symptomatic, the patient's primary care physician referred her to a gastroenterologist for suspected Crohn's disease. She underwent repeat colonoscopy to confirm the diagnosis. Terminal ileal ulcers were again seen and biopsy results revealed metastatic breast cancer.

**Discussion:** Breast cancer may metastasize anywhere within the GI tract. In one retrospective review, it was estimated that breast cancer metastasizing to the GI tract involved the small bowel in 19% of patients. The most common presentations that are reported are abdominal pain, obstruction and bowel perforation.

The differential diagnosis of terminal ileal ulcers is broad. The most common etiologies are inflammatory bowel disease, infections and ischemia. However, metastatic breast cancer may affect the small bowel although it is rare. Clinicians should have a high index of suspicion in patients with metastatic breast cancer presenting with terminal ileal ulceration.

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### Dysphagia in a Patient after Cervical Spine Surgery

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**Case:** A 66 year-old gentleman with a history of stroke and cervical spine surgery is referred for evaluation of dysphagia. His symptoms have been present for 10 days, and occur with solid food and pills. He reports some decreased oral intake and mild weight loss but denies odynophagia, abdominal pain or melena. His past history is significant for cervical spine spondylolisthesis for which he underwent cervical discectomy and stabilization via an anterior approach, performed 8 months prior to this presentation. On exam, his abdomen was benign and no cervical lymphadenopathy was noted. An upper endoscopy was performed which showed a normal stomach and duodenum. On withdrawal, the esophagus was examined carefully, revealing the finding below (Fig. 1). The image shows a screw from the patient's cervical hardware eroding into the upper esophagus, with the lumen seen at the bot-

tom of the image. A subsequent swallow study shows pooling of contrast in the area of erosion. The patient underwent surgical repair of the defect using a sternocleidomastoid flap.

**Discussion:** Pharyngo-esophageal perforation is a rare complication of cervical surgery. It is primarily associated with anterior-approach cervical surgery. The incidence is unknown, but in four large studies of anterior cervical surgery a total of 7 cases of perforation were noted. The presentation of this complication can range from complete lack of symptoms to mediastinitis and sepsis. Due to the wide variability in presentation, diagnosis can be difficult and a high index of suspicion should be maintained in patients with esophageal symptoms and a history of anterior cervical surgery. Perforation is thought to be mediated by recurrent infections or chronic compression of the esophagus and subsequent ischemia. Investigation can include lateral spine films, CT scan, swallow study or endoscopy. Management remains controversial, and ranges from conservative treatment with nasogastric tube, NPO status, and intravenous antibiotics to surgical intervention with an SCM flap. Given the rare nature of this complication, definitive guidelines for therapy have not been outlined, and further study is necessary before a standard approach can be recommended.[figure1]



739

### Endotherapy for Massive GI Bleeding Due to Duodenal Lipoma

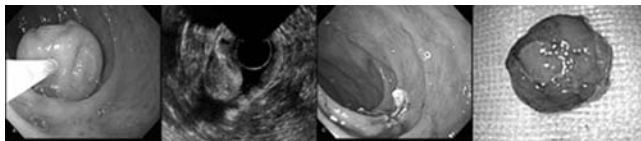
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Massive gastrointestinal bleeding due to duodenal lipoma is uncommon. We present here a case to demonstrate the feasibility of endoscopic treatment. A 64 y male presented to the ER with acute shortness of breath. He is obese, hypertensive, chronic smoker and has advanced COPD. He was hypotensive and cyanotic on admission. He was immediately intubated and transferred to ICU. Further workup revealed severe pulmonary embolism (PE). He was started on anticoagulation and was considered for thrombolysis. Within 6 hours he developed massive hematemesis and had a drop in hemoglobin by 3 gms/dL. There was no prior history of abdominal pain, NSAID ingestion, liver disease or alcoholism. He was immediately transfused with PRBCs, IV PPI. An EGD showed fresh blood clots in fundus and duodenum that could not be cleared. He was continued on PPI infusion and anticoagulation was continued without thrombolysis. Hematocrit was maintained with PRBCs. A repeat EGD revealed a polypoidal lesion with surface ulceration in 2nd part of duodenum (Fig. 1A). An upper endoscopic ultrasound (EUS) showed a well-defined, hyperechoic lesion arising from the submucosa, suggestive of lipoma. In view of significant bleeding and ongoing need for anticoagulation due to PE, this lesion was resected endoscopically. Histopathology confirmed it as a lipoma.

Submucosal lesions causing massive GI bleeding is uncommon but not rare. The differential diagnosis for submucosal lesions causing bleeding include

varices, vascular malformations (Dieulafoy's lesion), stromal tumors arising from muscularis mucosa and lipomas. Endoscopic appearances can sometimes be suggestive – arterial lesions may be pulsatile; varices may be indentable with the tip of a biopsy forceps; benign tumors may be firm and mobile under the mucosa. Echomorphology on EUS is generally confirmatory. Endotherapy of lesions detected incidentally on endoscopic examination is debatable. Endoscopic resection, avoiding surgery, is the treatment of choice for symptomatic patients.

Massive gastrointestinal bleeding due to duodenal lipoma is uncommon. Confirmation of echomorphology on EUS facilitates safe removal of these tumors by endoscopic resection.[figure1]



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#### Trouble Shooting in the Endoscopy Unit: Successful Management of Gastro-Gastric Fistula and Gastro-Jejunal Anastomosis Obstruction Using a Polyflex Stent

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A 50 year old man underwent Roux-en-Y gastric bypass (RNY GBP) for morbid obesity. Immediately post-op the patient was diagnosed with an anastomotic leak requiring revision of the gastro-jejunostomy anastomosis (GJA). Eight months later, he presented with protracted nausea and post-prandial emesis. An upper endoscopy revealed an obstructing giant marginal ulcer involving approximately 75% of the GJA. Despite optimal medical therapy (sucralfate, PPI, misoprostol, liquid diet) the ulcer persisted on repeat endoscopy 3 months later. During this endoscopy a second lumen was visualized in the gastric pouch which represented a gastro-gastric fistula (GGF). This tract was dilated followed by placement of a percutaneous endoscopic gastrostomy (PEG) tube for enteral nutrition in the excluded stomach. Subsequent endoscopy 2 months later showed a stenotic GJA with persistent ulcer. In an effort to facilitate resumption of oral intake and reverse the bariatric anatomy, we decided to place a Polyflex stent (Boston Scientific, Natick MA) across the GGF. To alleviate the sharp angulation between the gastric pouch and the excluded stomach a biliary guidewire was passed through the gastrostomy tube and subsequently withdrawn through the mouth. Keeping this wire in a state of constant tension at both ends (mouth and gastrostomy), a 23 mm wide × 90 mm long stent was successfully deployed across the GGF. To prevent stent migration the proximal aspect of the stent was affixed to the gastric mucosa using a resolution clip and a suture loop that was placed through the stent prior to assembly. The patient's symptoms abated completely after this procedure. The stent was successfully removed six months later. During his four months follow up, he continues to maintain good nutritional status with oral feeding alone.

**Discussion:** Prior to divided RNY GBP, GGF occurred in up to 50% of patients. Currently the incidence is 6%. GGF may be asymptomatic or present with failure to lose weight or weight regain. Marginal ulcers secondary to GGF necessitate addition of a PPI. Smoking and the use of NSAIDs are contraindicated to enhance mucosal healing. This case represents a novel successful off label use of the retrievable Polyflex stent with endoscopic reversal of bariatric anatomy to facilitate healing of an obstructing marginal ulcer and assure PO intake.

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#### A Case of Common Variable Immunodeficiency Mimicking Refractory Celiac Sprue

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**Case presentation:** A 57 year old Caucasian male with a history of common variable immunodeficiency (CVID) presented to our clinic for management of his celiac disease. The patient had been diagnosed in 2001 after presenting to an outside gastroenterologist with complaints of diarrhea and had evidence of scalloping and villous blunting on an EGD. The patient did not respond to a gluten free diet and lost 40 lbs despite the gluten restriction. Given the weight loss, radiological workup was performed (CT and small bowel follow through) but showed no abnormalities except for splenomegaly which may be found in patients with CVID. A repeat small intestinal biopsy in our institution showed evidence of extensive inflammatory infiltrate and submucosal fibrosis with no evidence of villous blunting. Flow cytometry was negative for lymphoma. A capsule endoscopy showed villous atrophy, decreased folds, mucosal erythema, and granularity along with lymphangiectasia. The patient's gastrointestinal symptoms as well as endoscopic and histologic findings were attributed to CVID and not celiac disease. He was started on intravenous immunoglobulin therapy. His symptoms improved, and he noted an increase in his weight after being taken off the gluten free diet. **Discussion:** Among the primary immunodeficiency disorders, gastrointestinal manifestations tend to predominate in patients with CVID. Histologically, CVID can mimic endoscopic findings suggestive of celiac disease. There are subtle differences, however, that gastroenterologists should be aware of in order to delineate between the two diseases as the management strategies are different. Plasma cells are absent from the intestinal biopsy specimens of patients with CVID, like our patient described above. Apoptotic bodies are common in CVID. A gluten free diet improves villous atrophy in approximately 50% of patients with CVID, while it normalizes villous architecture in the majority of patients with celiac sprue. Unlike CVID, celiac sprue, is associated with increased amounts of IgM and IgA. Treatment with immunoglobulin (IVIG) does not always appear to improve the rate of infection or improve GI symptoms in CVID, unlike our patient. Supportive treatment with fluids as well as repletion of vitamins and minerals remain a central part of therapy. In conclusion, this case illustrates the need for searching for alternative causes for diarrhea and malabsorption in a patient that is refractory to treatment for celiac disease.

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#### Unusual Presentation of a Cecal Volvulus

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**Introduction:** Cecal bascule is a rare type of volvulus where the cecum folds anteriorly, displacing the appendix into the RUQ. Although colonic obstruction usually presents as a surgical emergency, the diagnosis is usually not made preoperatively without radiography. This is an unusual presentation of cecal bascule.

**Case Report:** 81 y/o black female with diabetes presented with 4 days of "crampy" constant lower abdominal pain, constipation, vomiting and poor appetite. She denied bleeding, viral illness, smoking, antibiotic use, or prior abdominal surgery. Examination revealed tachycardia, diffuse abdominal tenderness especially RLQ, no peritoneal signs with a negative guaiac. After a bowel movement her pain improved (8/10 → 2/10).

Labs: Hgb 11.2 (nl MCV); WBC 7.7 (n-69%); Lactate 2.1; nl-AST /ALT; Amylase 67; Lipase 21.

The next 48 hours yielded alternating exam findings from a benign to surgical abdomen. Labs remained unchanged.

CXR: Right hemidiaphragm elevation with marked bowel distension in the RUQ.

CT scan: 9 cm cecum with an air-fluid level [figure1] Day two: Increasing pain with peritoneal signs warranted surgery. A dilated cecum was found folded onto the ascending colon into the RUQ, completely obstructed at the

fold with patchy necrotic areas requiring a right hemicolectomy. [figure2] Her post-op course was uneventful.



**Discussion:** Bascule is a French term meaning seesaw. This is appropriate as the cecum flips upward on itself causing a deep crease across the bowel and an occlusion of the gut lumen. Cecal bascule differs from volvulus in that its injury is not caused by vascular compromise, but by a one way flap-valve with pressure building against the fold distally. This case illustrates a unique condition and presentation of waxing and waning pain, reminding us that cecal bascule must be considered in patients with abdominal pain and distension.

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#### Adenocarcinoma of the Colon Associated with Esophageal Dysmotility

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An 80 year old woman presented with a 2 week history of worsening nausea and vomiting of gastric contents. She reported anorexia and 20 lb weight loss over one month. She denied dysphagia, odynophagia, globus sensation or regurgitation. A prior EGD showed gastritis with evidence of *H. pylori* that was treated. She was scheduled for colonoscopy but developed abdominal pain and vomiting with the bowel prep. Initial evaluation revealed stable vital signs and no fever. Physical exam was significant for a benign abdomen and fecal occult blood. There was mild anemia. A CT scan of the abdomen showed distention of the distal esophagus and no evidence of bowel obstruction. A gastric emptying study demonstrated no transit of solid food from the esophagus into the stomach at 90 minutes after ingestion. A repeat EGD showed a dilated distal esophagus with retained food particles and no evidence of stricture. The stomach and duodenum were normal. Biopsies were

unremarkable. The vomiting persisted despite metoclopramide therapy. Subsequent colonoscopy showed a circumferential mass in the sigmoid colon. The patient underwent sigmoid resection and pathology revealed adenocarcinoma. Post-operatively the patient experienced no further symptoms and she was discharged home in stable condition.

GI dysmotility is a rare paraneoplastic syndrome that occurs most often in association with small cell lung carcinoma. Rarely lung adenocarcinoma, leiomyosarcoma, lymphoma, melanoma and cancers of the kidney, breast and prostate have been implicated. Patients often suffer from intestinal pseudo-obstruction. Dysphagia, bladder dysfunction, autonomic insufficiency and peripheral neuropathy have also been described. The onset of symptoms may precede the discovery of the primary tumor by several years. It is thought to have an autoimmune basis and histology typically demonstrates marked lymphocytic infiltration of the myenteric plexus. The interstitial cells of Cajal may be a target in the pathogenesis of this disorder. Cross-reacting autoantibodies found in the sera of these patients bind to the primary tumor cells and to neuronal cells in the myenteric plexus, resulting in inflammation and destruction. The detection of circulating anti-neuronal nuclear antibodies in the serum may aid in the diagnosis of this condition.

We report here a case of colonic adenocarcinoma associated with esophageal dysmotility as a paraneoplastic syndrome which resolved after resection of the tumor. This has not been previously reported in the literature.

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#### Chlorzoxazone as the Cause of Fulminant Hepatic Failure

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A 48-year-old Caucasian woman with a past medical history of anxiety presented to the emergency room complaining of 3 weeks of jaundice, nausea, and right upper quadrant pain. She had no significant family history. She rarely drank alcohol and did not use illicit drugs. Medications were escitalopram, which she had been on for several years, and chlorzoxazone 250 mg three times daily, which she had been taking for the last 4 months for shoulder pain.

On exam the patient was jaundiced, with scleral icterus. She had a tender right upper quadrant. She had no stigmata of chronic liver disease. She did not have evidence of encephalopathy on admission.

Laboratory data: WBC 9,600 mm<sup>3</sup>; Hgb 12.7 g/dL; Platelets 243 × 10<sup>3</sup>/uL; PT 37 sec; INR 3.8; Creatinine 0.9 mg/dL; Albumin 2.7 g/dL; Total bilirubin 18 mg/dL; Direct bilirubin 12.9 mg/dL; AST 923 U/L; ALT 1391 U/L; AlkP150 U/L. HBsAg, Hep C Ab and HCV PCR were negative. Hepatitis A IgM negative, IgG positive. ANA and SMA negative. AMA positive at 1:160, LKM and SLA were negative. CMV negative. Acetaminophen level was undetectable on admission.

Ultrasound revealed a mildly heterogeneous liver with no focal masses and appropriate flow in all vessels.

Transjugular liver biopsy: Sub massive hepatic necrosis with severe interface activity and widespread reticulin collapse, severe cholestasis, intense ductular proliferation, marked neutrophilic infiltrate due to chemotactic response to ductular proliferation, occasional eosinophils and few plasma cells, not suggestive of autoimmune hepatitis, moderate ductopenia, no cholangitis. CMV, herpes, and hepatitis B immunostains were negative.

The patient was admitted for evaluation of acute liver failure. Chlorzoxazone was discontinued. Over the course of 8 days, transaminases decreased but PT remained elevated. She had very low Factor 5 and 7 levels which continued to decrease during her stay in the hospital (down to <1%). Patient developed stage 2 encephalopathy and was listed for liver transplantation. Seven days after being listed, the patient underwent successful liver transplantation.

Chlorzoxazone is a centrally acting muscle relaxant introduced nearly fifty years ago. Hepatotoxicity is a known rare adverse reaction. Literature review reveals two deaths attributed to liver failure from chlorzoxazone, and one other patient survived after liver transplant from chlorzoxazone-induced

liver failure. This case reemphasizes the need to monitor for hepatotoxicity in patients taking chlorzoxazone.

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#### Ulcerative Jejunoileitis – An Uncommon Cause of Gastrointestinal Bleeding and Adenopathy

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A 66 year old man presented for unexplained gastrointestinal bleeding. He had noticed bright red blood per rectum and had a syncopal event upon getting up from the toilet. His initial evaluation included an EGD and a colonoscopy without any significant findings. He required 5 units of blood and was discharged and sent to Boston University Medical Center for a small intestinal evaluation. Of note, he was noticed to have a 45 pound weight loss over the prior months and he had an albumin of 2.7 g/dl. His past medical history was significant for hypertension, coronary artery disease and diabetes, and he was not taking any NSAIDs. On exam, he was tender at a site of fullness in the right lower quadrant. His laboratory evaluation revealed an elevated WBC of 11.6 and ESR of 87 with a normal tTG and IgA level and HIV negative. A CT enterography was performed showing multiple enlarged paraaortic lymph nodes up to 2.6 cm. Additional prominent less than one centimeter lymph nodes were noted within a region of swirling mesentery anterior to the pancreas. Concentric wall thickening was noted in multiple loops of the distal ileum and less so in some loops of jejunum. The patient underwent a CT-guided lymph node biopsy. The pathology, flow cytometry and PCR of the lymph node biopsy were inconclusive (non-specific inflammation). All other laboratory cell-typing evaluations for lymphoma were negative.

Without a definitive diagnosis, a capsule endoscopy was performed and demonstrated multiple ulcerations scattered throughout the small intestine. The proximal ulcerations were within the reach of a push enteroscope and were biopsied. The pathology was inconclusive (normal small bowel mucosa). The patient underwent a CT/PET scan that was essentially negative except for a mild uptake presumed to be from the jejunal biopsies.

After another bleeding episode, the patient was taken to the operating room. An area of significant ileal inflammation and adjacent adenopathy was easily identified and was resected laparoscopically. Pathology demonstrated mucosal ulcerations with reactive adenopathy without granulomata, lymphoproliferative disease or carcinoma, suggestive of primary ulcerative jejunoileitis. Ulcerative jejunoileitis is a rare disease entity and can be seen without the presence of associated celiac disease. The significance of the adenopathy, weight loss, and hypoalbuminemia suggested a neoplastic process that required an operation to make a definitive diagnosis.

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#### Lung Cancer Presenting with Dysphagia Due to Esophageal Metastasis

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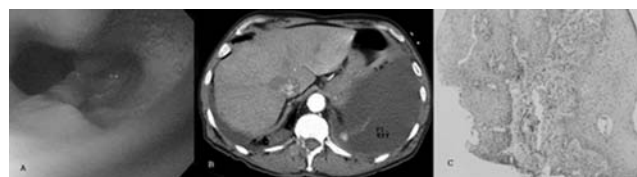
Esophageal metastases are rare and majority of them originate in the larynx, hypopharynx, trachea, bronchus and stomach. We report a case of lung cancer presenting with dysphagia.

A 58 year old white male complained of intermittent dysphagia to solids for 7 weeks. He denied anorexia, but lost 15 lbs in 6 months. He is a chronic smoker (100 pack years) but denied any alcohol or drug use. Chest x-ray showed left sided pleural effusion. EGD revealed extrinsic compression in mid esophagus and a 2 cm cratered ulcer (Fig. 1A). Thoracic CT revealed left pleural effusion (pl. eff), T12 vertebral metastases impinging on the cord (>>) and mediastinal lymphadenopathy (Fig. 1B). Esophageal ulcer

biopsy showed atypical cells in the sub-epithelial stroma (Fig. 1C). Immunohistochemistry was consistent with lung primary. Metastatic spread was also confirmed from vertebral lesion and the pleural fluid. He was treated with steroids, spinal irradiation and chemotherapy with Docetaxel. However, patient succumbed to an acute coronary event one week later.

Tumors metastasizing to the esophagus include gastric, renal, hepatocellular, prostate, testicular, skin and bone. Autopsies in patients dying of cancer suggested an overall incidence of 3 to 6%, with breast and lung as the most common primary tumors. Secondary esophageal involvement occurs due to (i) direct extension (most common), (ii) lymphatic or, (iii) hematogenous spread. 1–2% of lung cancer patients initially complain of dysphagia. Spread to the esophagus results in sub-mucosal infiltration with normal overlying mucosa and endoscopic biopsies are usually non-diagnostic. However, in the present case esophageal ulcer biopsies were diagnostic of metastases from lung.

Recent onset dysphagia in a chronic smoker warrants urgent EGD to exclude esophageal cancer or rarely metastases from lung cancer.[figure1]



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#### Endoscopic Treatment of a Small Bowel Obstruction – Removal of an Apricot-Pit Bezoar

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A 94 year old woman developed acute onset of nausea, vomiting, significant abdominal distention, and chest pain. Her history was limited by progressive memory loss and limited short term recall. However, her daughter (a physician) reported that she may have swallowed an apricot pit. Her past medical history is noteworthy for severe coronary artery disease with congestive heart failure, cerebrovascular accidents and hypertension.

On examination, the patient was hemodynamically stable, and she had a distended, tender abdomen, and a succussion splash. While ruling out cardiac causes of her pain, radiographs of the abdomen demonstrated several mildly dilated loops of small bowel with little to no gas in the colon, suggesting a small bowel obstruction. A subsequent CT scan demonstrated moderate dilatation of the stomach and loops of proximal small bowel, with collapse of the terminal ileum. There appeared to be a short segment of narrowing in the ileum that likely represented the mechanical obstruction; a heterogeneous intraluminal collection of gas and soft tissue was located proximal to this site, and its appearance was compatible with a bezoar.

The patient's cardiopulmonary conditions were treated during the next 24 hours, and her abdomen became progressively more distended while her discomfort increased. In addition, her lactic acid level rose to 2.6 (ULN 2.0). A repeat CT scan revealed increasing dilatation of the proximal small intestine. The patient and her daughter ardently hoped to avoid an operation, so we proposed an attempt at removing the bezoar via endoscopy.

Following two tap water enemas, an endoscope was passed through the stool-filled colon and into the terminal ileum under minimal sedation. Anticipating a poorly prepped colon, the plan was to start with a pediatric colonoscope with the double balloon endoscope as a back-up that was subsequently not needed. About 40 cm proximal to the ileocecal valve, an obvious obstructing foreign body was identified and dragged into the colon with a snare. This 8-cm long bezoar was compatible with the apricot pit, and her abdomen immediately deflated. The endoscope was re-inserted and we observed no



strictures or mucosal narrowing; some superficial erosions most likely reflected ischemic changes from the formerly impacted bezoar.

This poor surgical candidate underwent an endoscopic removal of an apricot-pit bezoar, with immediate relief of an acute small bowel obstruction. She has been subsequently well.

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# **A Case of Painless Jaundice as the Primary Presenting Symptom for Renal Cell Carcinoma**

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**Introduction:** Renal cell carcinoma (RCC) is regarded as one of the great masqueraders in medicine. This is a case of an unusual presentation for this malignant entity.

**Case:** A 69-year-old male presented with a 3 week history of diffuse pruritis, progressive jaundice, dark urine, and clay colored stools. The patient had no abdominal pain or fever. Laboratory studies were consistent with cholestasis: AST 237 U/L, ALT 245 U/L, Alk Phos 689 IU/L, total bilirubin of 16.7 mg/dL, and direct bilirubin of 11.2 mg/dL. The patient was afebrile, diffusely jaundiced, and had no abdominal tenderness on exam. Magnetic resonance imaging of the abdomen and magnetic resonance cholangiopancreatography revealed a 10 cm × 8 cm × 7 cm left renal mass and retroperitoneal and portocaval lymphadenopathy. A 3 cm × 2 cm retropancreatic node displaced the pancreatic head and mechanically obstructed the extrahepatic common bile duct (CBD) causing intra- and extrahepatic biliary ductal dilation. Endoscopic retrograde cholangiopancreatography (ERCP) was performed the following day. A very tight mid-CBD 2 cm long stricture consistent with extrinsic compression was found (see Figure). Biliary stricture dilation was performed and a biliary stent (10-French 9-cm straight Cotton-Leung biliary stent) was placed in position across the stricture with excellent biliary drainage. Subsequently (2 weeks later) the patient had left radical nephrectomy and mobilization of the liver and partial lymphadenectomy. The patient is currently undergoing chemotherapy and has had one planned biliary stent change since surgery.



**Discussion:** Painless jaundice has been infrequently reported in the literature as a presenting or associated complaint with renal cell carcinoma. Reported causes have included metastases to: pancreas or surrounding lymph nodes (2 cases and 2 studies of 5 patients each), intraluminal common bile duct (2 cases), and duodenum (one case). Additionally, 2 cases of jaundice secondary to a paraneoplastic syndrome associated with RCC have been

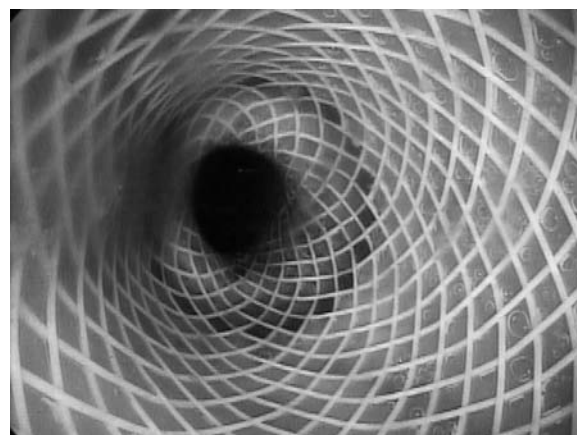
reported. This case, along with those previously reported, demonstrates that while rare, an inclusive differential for painless jaundice may uncover alternative primary pathology.[figure1]

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# **Successful Removal of a Migrated Esophageal Self-Expanding Metallic Stent from the Stomach with the Aid of an Esophageal Self-Expanding Plastic Stent**

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Self expanding metallic stents (SEMS) have been useful for palliative treatment of malignant esophageal obstruction, however, occasionally migration of the stent occurs. Extraction of migrated metal esophageal stents can be a challenging procedure with complications including esophageal perforation and hemorrhage. We describe an innovative way of successfully extracting a migrated esophageal SEMS from the stomach 7 weeks after initial deployment, using a self expanding plastic stent (SEPS) as a funnel to protect the strictured distal esophagus.



A 63 year old male with stage IV esophageal adenocarcinoma causing stricture of the distal 5 cm of the esophagus, underwent successful deployment of an Ultraflex SEMS (12 cm in length) across the stricture. Seven weeks after deployment, the stent was seen migrated into the stomach. A pediatric upper endoscope was unable to traverse the stricture, thus a balloon dilation was performed of the stricture and the scope was then advanced into the stomach. The SEMS was too large to be pulled through the stricture. Attempts to cross the stricture with overtubes and a foreign body hood protector were

unsuccessful due to the anatomy of the stricture. The initial procedure was terminated and a repeat attempt was performed two days later. A self-expanding plastic stent (SEPS) was deployed with the proximal flare (21 mm diameter, 9 cm length, 25 mm diameter flare) in towards the stomach to act as a funnel, as well as to protect the esophageal mucosa (Fig. 1). The stent was successfully placed across the stricture. The endoscope was advanced through the stent and the end of the SEMS was grabbed with a jumbo snare. The SEMS was pulled through the SEPS and out of the patient returned to recovery in stable condition (Fig. 2).[figure1][figure2]

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### Is It Time To Perform HIV Screening among Patients Prior to Receiving Infliximab (Remicade) Therapy?

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**Background:** Infliximab (Remicade), a TNF-alpha inhibitor, is primarily used in the treatment of autoimmune disease, as well as inflammatory bowel disease. We describe a case of infliximab therapy initiated in a man with ulcerative colitis (UC), who developed cytomegalovirus (CMV) retinitis, due to undiagnosed HIV/AIDS.

**Case report:** A 65 year old Caucasian man with past medical history of hypertension, diabetes mellitus and otherwise healthy, was referred to the gastroenterologist office for complaints of diarrhea, rectal bleeding and recent weight loss. Infectious etiology was ruled out with negative stool studies; he then underwent a colonoscopy, revealing diffuse erythema and exudate consistent with panulcerative colitis. Subsequent treatment with prednisone, mesalamine, and 6-MP gave some symptomatic relief. Due to an inability to completely wean off prednisone the decision was made to start infliximab therapy after a negative tuberculin skin test. After initial induction with infliximab the patient showed marked improvement of his GI symptoms. He was continued on a maintenance regimen of infliximab. Several months later he presented to his physician's office with the complaint of decreased vision, and seeing floaters in his right eye. After a referral to a specialty ophthalmology center the diagnosis of CMV retinitis was made. Since CMV retinitis is associated with HIV/AIDS, he underwent testing for HIV. The test was positive with a viral load of 201,000-copies/ml and CD4 count of 68-cells/mm<sup>3</sup>. By this time, infliximab had been stopped; he received treatment for his CMV retinitis, which eventually necessitated the placement of a ganciclovir intraocular implant, and antiretroviral therapy for HIV/AIDS.

**Discussion:** An increased risk of developing serious infections is seen in patients on an immunosuppressive agent such as infliximab. Currently it is recommended that all patients be screened for TB prior to initiation of therapy. Our patient was a healthy man with no obvious risk factors for HIV/AIDS. The immunosuppressive effects of infliximab could potentiate opportunistic infections in patients with HIV. Patients are not always forthcoming with details of their sexual history, or may not be aware of potential risk factors for HIV. Mandatory HIV testing prior to initiation with infliximab would have prevented the CMV opportunistic infection in this patient. We propose that HIV testing should be offered to all patients prior to initiating therapy with infliximab.

## 751

### Hepatocellular Carcinoma in a Patient with Hepatitis C in the Absence of Cirrhosis

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Chronic infection with hepatitis C virus (HCV) is regarded as a risk factor for hepatocellular carcinoma (HCC). Current guidelines recommend screening patients with HCV for HCC only if there is evidence of cirrhosis. HCC has

been described in HCV patients without cirrhosis, but to our knowledge data has been very limited.

We report this case of an 81- yrs old African American female with a history of HCV infection, the only risk factor being a blood transfusion in 1970. She presented with abdominal pain, and was found to have 4.2 × 4.6 cm enhancing lesion in the left lobe of the liver by computed tomography (CT-scan) of the abdomen. Subsequently, a CT-guided fine needle aspiration (FNA) was positive for malignant cells. Testing for hepatitis B surface antigen (HBsAg) was negative, patient had no history of exposure to toxins and denied alcohol intake. The patient had no evidence of cirrhosis clinically or by labs (Total Bilirubin; 0.6 mg/dl, international normalized ratio (INR); 1.1, albumin of 3.7 g/L and platelet count of 220 × 109/L). Since the patient was not considered a candidate for liver transplant given her age, she underwent surgery, and was found to have a 6 cm hepatoma for which she had a left hepatic lobectomy. Pathology revealed mild to moderately differentiated hepatocellular carcinoma with cancer free margins. Histological examination of the cancer free hepatic tissue showed mild chronic inflammation with hepatosteatosis and no evidence of cirrhosis or fibrosis. One year post surgery, patient continues to be fully functional and has normal synthetic liver function with no evidence of recurrence.

This case raises the possibility that patients with chronic hepatitis C infection, without evidence of cirrhosis who are currently considered to be at low risk for HCC may also develop HCC. Whether the long duration of infection has a role, needs to be evaluated further. The natural history of hepatitis C is still evolving and as longer follow up after the initial infection becomes available, new long-term effect of the infection may be observed.

## 752

### Encapsulating Peritoneal Sclerosis: A Rare, but Recognized Cause of Ascites in Patients with Renal Failure

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Encapsulating peritoneal sclerosis (EPS) is a rare but devastating complication of peritoneal dialysis (PD), occurring typically, but not exclusively after renal transplantation (RT). Clinical features include abdominal distention with ascites and/or intermittent small bowel obstruction (SBO). Diagnosis may be difficult to establish because the condition is rare and the index of suspicion may not be sufficiently high.

A 37 year-old man underwent live donor RT during 1995 for hypertensive nephroclerosis. Immunosuppressive therapy comprised cyclosporin, azathioprine and prednisone. Four years later, renal failure recurred after repeated episodes of allograft rejection; he underwent transplant nephrectomy and started PD, converting to hemodialysis in 2006. He complained of increasing abdominal distention, early satiety, intermittent vomiting of two months' duration and 15 lb. weight loss, earlier this year. There was no remote history of jaundice or family history of liver disease; he had no risk factors for hepatitis B or C virus exposure. Phenytoin was being taken for seizure prophylaxis. Physical examination revealed evidence of recent weight loss, and ascites, but no icterus or other clinical features of cirrhosis and portal hypertension. Mental state was normal. Laboratory data were as follows: Albumin 2.8 g% (normal range [NR]: 3.4–4.5), bilirubin 0.2 mg% (NR: 0.2–1.2), prothrombin time 12.2 sec (NR: 11.1–13.1), aspartate aminotransferase 11 IU/L (NR: 10–60) and alkaline phosphatase 162 IU/L (NR: 30–135). His calcium concentration was 8.6 mg% (NR: 8.7–10). There was no evidence of chronic hepatitis B or C virus infection; his serum ferritin concentration was 667 ng/mL (NR: 30–300). Liver histology revealed no inflammation or fibrosis, but the presence of some iron within Kupffer cells consistent with dialysis-dependent renal failure. The serum-ascites albumin gradient was 1.8 g%. Contrast-enhanced CT scan confirmed the presence of large, loculated intrabdominal fluid collections, causing compression of the second duodenal part. Thickening of the peritoneum consistent with a chronic inflammatory process was evident also. A presumptive diagnosis of EPS was made. Treatment with prednisone (30 mg/day) and tamoxifen (20 mg, bid) was begun, pending possible surgery.

The clinical features of EPS may suggest other potential diagnoses, e.g. mechanical SBO or end-stage liver disease. However, the combination of PD, before or after RT, abdominal distention and vomiting should not be overlooked.

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### The First Reported Case of Disseminated *Coccidioides* Involving the Esophagus and Presenting with Severe Iron-Deficiency Anemia

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**Introduction:** *Coccidioides* infections have been documented in many organs of the body, but the only case of gastrointestinal tract involvement reported thus far is a single case of retropharyngeal abscess. Here, we present a case of disseminated *Coccidioides* affecting the esophagus.

**Case:** A 68-year-old Hispanic man presents with 3 years of progressive worsening weakness and fatigue, and 40 pound weight loss in the last 3 months. He has also taken 3-years of naprosyn for chest pain. He did not report any hematochezia, melena, or hematemesis. Past history included Billroth II for peptic ulcer disease. Patient reports history of suspicious lung mass on chest radiograph 8 months ago when he was found to have pneumothorax. Patient lived near the border of Arizona and Mexico for 30 years as a lemon farmer prior to moving to San Bernadino, California recently.

On exam, the patient was very thin. His Hgb was 4.6, ferritin 4.5, TIBC 407, and iron 8, and he required 6 units of PRBC transfusion. EGD and colonoscopy were performed and revealed a 1.5 cm deep esophageal ulcer with raised borders at 35 cm with pathology showing acute and chronic ulceration containing fungal spores of *Coccidioides immitis*. Chest CT revealed multiple deep neck and chest lymphadenopathy, left clavicular soft tissue mass, and soft tissue mass adjacent to T6, T7 and L2 vertebral bodies. A calcified lymph node was also seen adjacent to the deep esophageal ulcer at 35 cm. Bronchoscopy and ultrasound-guided FNA of perijugular lymph nodes reported only inflammatory changes and no malignancy. *Coccidioides* Ab serology was 1:128. CSF *Coccidioides* serology and cultures were negative. HIV screen was also negative. The patient was treated with 10 days of IV diflucan followed by oral diflucan and subsequently discharged home with infectious disease, gastrointestinal and neurosurgery follow-up.

**Conclusion:** This is the first reported case of disseminated *Coccidioides* infection involving the esophagus and the second case in literature involving the gastrointestinal tract. The CT scan suggests a localized dissemination of *Coccidioides* from chest lymphadenopathy to the esophagus, causing a deep esophageal ulcer. The initial finding of severe anemia is also a unique presenting feature of this case.

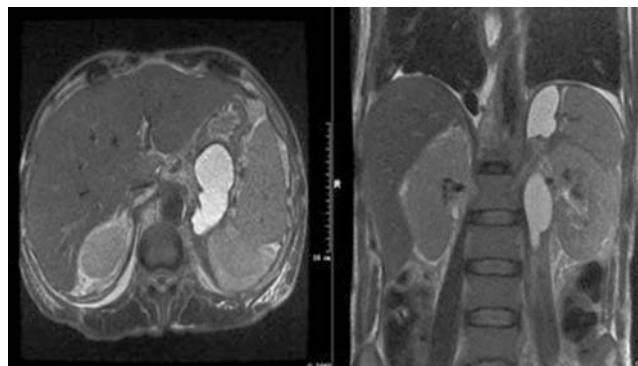
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### Pancreatic Pseudocyst Dissecting into the Psoas Muscle

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We describe an unusual extension of a pseudocyst into the psoas muscle. A 56 year old male with history of chronic pancreatitis presented with epigastric pain and tenderness. His serum amylase and lipase were within normal limits. A CT scan of the abdomen demonstrated several cystic structures with peripheral enhancement in the lesser sac consistent with pseudocyst formation and cystic lesion within the psoas muscle. An MRCP demonstrated the connection between these cysts.[figure1] Percutaneous drainage of the pseudocyst was performed.

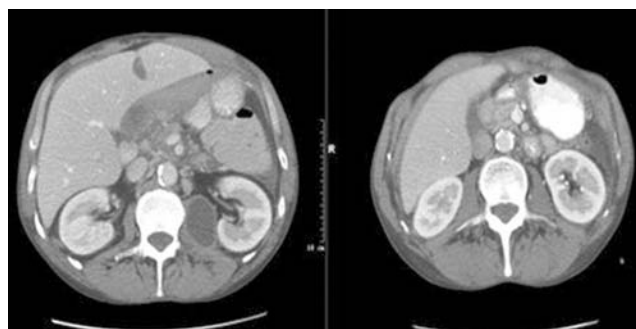
A follow up CT scan 15 days later showed a reduction in size of the pseudocyst within the psoas as well as that in the lesser sac as shown in the figure which compares the size of the psoas pseudocyst before and after the



#### Aspirate Fluid analysis

Amylase	7,190 u/L
Lipase	11,883 u/L
Culture	No growth
Cytology	Negative for malignant cells

procedure.[figure2]The drain was removed after a few days and the patient had an uneventful recovery.



Although pancreatic pseudocysts are usually found in the vicinity of the pancreas, there are reports of them occupying unusual sites such as the mesentery, mediastinum and spleen. A review of literature revealed three cases of pancreatic pseudocyst extending into the psoas muscle. Two of them were alcoholics who presented with pain in the hip without any signs or symptoms of pancreatitis. Both were diagnosed by CT of the abdomen and were treated by percutaneous drainage. Fluid analysis yielded a negative culture with amylase of >10,000. The third case presented as a swollen and painful left thigh and raised serum amylase which was treated by laparotomy. Our case adds to the existing literature regarding the feasibility of percutaneous drainage in the management of pseudocyst pancreas extending into the psoas.

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### Rifaximin for the Treatment of Newly Diagnosed Crohn's Disease

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An aggressive immune response to commensal enteric bacteria is thought to contribute to the pathophysiology of Crohn's disease in genetically predisposed individuals. Rifaximin is a nonabsorbable antibiotic with broad-spectrum activity against intestinal pathogens, and multiple studies have demonstrated a clinical benefit with rifaximin in patients with mild-to-moderate Crohn's disease. This case series evaluated the effectiveness of

rifaximin monotherapy in patients (N = 2) with newly diagnosed Crohn's disease. Case report 1: a 25-year-old female presented with a 4-month history of chronic abdominal pain and diarrhea. A colonoscopy revealed a healthy colon to the ileum; however, a colonic biopsy was positive for non-caseating granuloma active ileitis. Small bowel capsule endoscopy showed numerous aphthous ulcerations, fissuring, and denudation of the small intestinal mucosa. Based on gastrointestinal (GI) symptoms and endoscopic findings, the patient was diagnosed with a baseline Crohn's disease activity index (CDAI) score of 260. The patient began therapy with oral rifaximin 400 mg twice daily (b.i.d.). After 5.5 weeks of rifaximin treatment, the patient experienced complete relief of GI symptoms, and endoscopic findings revealed substantial healing of the small intestinal mucosa (CDAI score = 18). The patient has remained asymptomatic with rifaximin 800 mg/d for 7 weeks. Case report 2: a 25-year-old female presented with severe iron-deficient anemia as her only symptom. However, a colonic biopsy was positive for lymphoid nodular hyperplasia and her C-reactive protein (CRP) serum level was substantially increased (14.7 mg/L), indicating inflammation. Small bowel capsule endoscopy findings were characteristic of Crohn's disease, including numerous aphthous ulcerations, fissuring, edema, and active bleeding in the small intestine. The patient began therapy with oral rifaximin 400 mg b.i.d. After 4 weeks of rifaximin treatment, the patient's CRP level improved substantially (1.3 mg/L) and capsule endoscopy demonstrated healing of the small intestinal lesions. After 5 weeks of rifaximin 800 mg/d, the patient remains free of GI symptoms and has experienced stabilization of her severe anemia. In summary, rifaximin effectively improved clinical symptoms and promoted healing of the small intestinal mucosa for 2 patients with newly diagnosed Crohn's disease. These findings provide further evidence of the beneficial role of rifaximin for treatment of inflammatory bowel disease, warranting further investigation in controlled clinical trials.

## 756

**Exophytic Splenic Cyst Mimicking a Gastric Mass**

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A 15 year old male with a four year history of Crohn's Disease presented with unrelenting nausea, severe abdominal pain, anorexia, and a 15 lb weight loss. Despite therapy with Prevacid, azathioprine, and oral steroids, symptoms persisted. He underwent EGD and colonoscopy. During EGD, a 1.5-cm firm submucosal nodular lesion was visualized in the gastric cardia. Remainder of upper endoscopy was normal. The colon appeared diffusely erythematous with deep erosions and ulcerations present throughout. Gastric biopsies over the lesion revealed chronic active gastritis with *H. pylori*. Based on the appearance of the submucosal gastric mass, the differential diagnosis included enteric duplication cyst, stromal tumor, leiomyoma/leiomyosarcoma, pancreatic rest, and splenic cyst. To further classify this lesion, MRI of the abdomen was performed. The MRI revealed a 1–1.5 cm exophytic splenic cyst in the left upper quadrant which appeared to impress on the posterolateral aspect of the gastric fundus. No abnormality of the gastric wall was identified. The patient was subsequently admitted and treated with IV steroids and Infliximab for the diagnosis of Crohn's flare. The patient was also started on therapy to treat *H. pylori*. Symptoms improved and the patient was discharged. Given the small size of the splenic cyst and improvement in symptoms, the lesion was not surgically removed.

Splenic cysts are an unusual finding in the pediatric population; however, they should be considered in the differential of a gastric submucosal mass. There are no previous reports of a splenic cyst in a pediatric patient mimicking a gastric mass at the time of upper endoscopy. These lesions may be congenital or secondary. Secondary causes include chronic parasitic infection and abdominal trauma. It is important to recognize these lesions due risk of spontaneous rupture or abdominal pain caused by impingement on other intra-abdominal structures. The definitive treatment of these lesions involves partial or total splenectomy. Decision about surgical intervention is based upon the location and size of the cyst. In this case, the decision was made

the monitor the patient closely with serial imaging studies as abdominal pain improved significantly with treatment of underlying Crohn's disease and *H. pylori*. Should this splenic lesion grow rapidly, surgical consultation may be advised.

## 757

**Endometriosis Presenting as Recurrent Massive Ascites**

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Endometriosis typically presents as dysmenorrhea, pelvic pain, dyspareunia, and infertility. Less common clinical presentations of endometriosis from implantation on the kidney, lung, or colon include hematuria, pleural effusions and hemoptysis and gastrointestinal bleeding. Ascites complicating endometriosis is rare. We report an unusual case of endometriosis presenting as recurrent massive ascites.

A 30 year old African-American woman with worsening abdominal pain and distension over 2 months presented to the emergency room. The patient had a history of abdominal distension and pain occurring with every menses for several years. The symptoms had always resolved at the end of each menstrual cycle. Over the two months prior to presentation, the abdominal distension did not subside. After developing worsening abdominal pain, she presented to the emergency room for evaluation. She denied any nausea, vomiting, diarrhea, jaundice, or fever. Past medical history was significant for an elective abortion 7 years prior. Menarche had occurred at age 13 with subsequent regular cycles, no excessive bleeding. On physical examination, she was a healthy female in mild distress. She has a grossly distended abdomen with mild diffuse non-localizing abdominal tenderness, no stigmata of liver disease and no lower extremity edema. Laboratory studies were significant for a mild normocytic anemia. The remainder of the laboratory findings, including liver function tests, was normal. CA-125 was within normal limits. Pregnancy test was negative. Computer assisted tomography of the abdomen and pelvis revealed ascites, but no other significant intra-abdominal pathology. A paracentesis was performed. Four liters of serosanguinous fluid was aspirated. Fluid white cell count was 1650 cells/mm<sup>3</sup> with a differential of 88% neutrophils. Red blood cell count in the fluid was 110,000 cells/mm<sup>3</sup>. Fluid albumin was 3.2 g/dL, total protein 5.4 g/dL. Cytology was negative. With an absence of an etiology for the ascites, the patient underwent diagnostic laparoscopy. Laproscopic exam was grossly normal, random biopsies revealed endometrial proliferative tissue.

This case demonstrates that endometriosis should be considered in the differential diagnosis of ascites. The diagnosis may be difficult, and as this case demonstrates, random biopsies of the peritoneum may be necessary in establishing the diagnosis.

## 758

**Enteryx: Migration into the Lymphatics and beyond**

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**Introduction:** Endoscopic implantation of a biocompatible nonresorbable copolymer (Enteryx; Boston Scientific Corp, Natick, MA) was approved by the FDA in April 2003, as an effective therapy for gastroesophageal reflux disease (GERD). This technique injects 3–6 cc of Enteryx through a sclerotherapy needle into the lower esophageal sphincter (LES). The solution polymerizes into a spongy material shortly after injected and is not removable. In September 2005, the FDA recalled Enteryx due to complications associated with these polymer injections.

**Case:** A 39 year old white male with a history of GERD refractory to proton pump inhibitor (PPI) therapy presented with atypical chest pain for 2 years. Two years prior to presentation, patient underwent an Enteryx injection with good initial success. However, the patient has complained of intermittent,

sharp chest pain that has worsened since his procedure. Pain is not consistent with GERD symptoms and cardiac work up was negative. Past medical history, physical exam and labs were unremarkable.

With concern for a potential Enteryx-related complication, an appropriate work up was initiated. Upper endoscopy and upper gastrointestinal series were normal. A Computed Tomography scan of the chest, abdomen and pelvis, as expected, revealed polymer around the gastroesophageal junction. Unexpectedly, there was a hyperdense focus seen in the subcarinal region (Fig. 1) and another seen in the right hilum, consistent with polymer migration. Polymer was also found in small bowel wall.

**Discussion:** Polymer migration is a known complication of Enteryx, but no known reports of migration into the lymphatic system. Unrecognized transmural injections are a serious adverse event of Enteryx, as endoscopists may blindly inject into adjacent structures. Our patient likely had Enteryx injected into his lymphatic system, which quickly migrated to the subcarinal and right hilar regions before solidifying. It is unclear whether the polymer is responsible for our patient's current symptoms, but it is a possibility. Even though this product is no longer being used, it is important for gastroenterologists to be aware of the associated complications and appropriate work up of these patients.[figure1]



## 759

#### A Rare Case of Solid Pseudopapillary Tumor of the Pancreas in a Young Girl with Celiac Disease

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Solid papillary cystic tumors of the pancreas are rare entities and occur more frequently in women aged 20–40.

We report a case of a 11-year old girl followed for celiac disease (CD) with a secondary diagnosis of a pseudocystic pancreatic tumor.

This young girl was diagnosed with CD at the age of 9 after complaints of abdominal discomfort in the previous two months. Her sibling had been diagnosed with CD a few years earlier. Both her immunological work up and histological specimens were consistent with CD. In the following year her immunological tests progressively normalized, but her weight did not improve and her spine had to be evaluated for severe scoliosis. During work up an abdominal mass was noted.

Subsequent evaluations identified a solid papillary cyst tumor of the pancreatic head. She was then operated on and the mass was fully enucleated. Histological findings confirmed the diagnosis and showed that the margins

were free of disease. The latest abdominal ultrasounds have showed regular findings apart from two residual portal lymphatic nodes. She is now receiving pancreatic enzyme supplementations on the regular basis.

This is the first case of a rare solid papillary tumor of the pancreatic head occurring in a young girl who also carries the diagnosis of CD.

## 760

#### Progressive Liver Involvement with Multiple Myeloma Causing Non-Obstructive Cholestasis Despite Thalidomide and Dexamethasone Therapy

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A 49 year old male was diagnosed with kappa light chain multiple myeloma by bone marrow biopsy after presenting with acute renal failure and circulating plasma cells in the blood. He was started on thalidomide and dexamethasone. After receiving four cycles over a 3 months period, he had improvement on the peripheral blood smear but no response on repeat bone marrow biopsy. One month after initiation of therapy he started developing a gradual increase in total and direct bilirubin. The treatment was stopped 2 months later and the patient was admitted to the hospital for further work up after a total bilirubin reaching 9.4 mg/dl. Ultrasound of abdomen showed significant liver enlargement over a period of 2 months with no evidence of biliary obstruction. HIDA scan showed delayed hepatic uptake consistent with severe hepatocellular dysfunction. Transjugular liver biopsy demonstrated massive involvement with plasma cells. The immunoprofile in the liver biopsy was similar to that in the bone marrow biopsy supporting the diagnosis of hepatic multiple myeloma. During his 2 weeks of hospitalization the patient rapidly developed hepatic failure and was discharged home on hospice.

Plasma cell infiltration of the liver can be detected in 30 to 40% of patients with multiple myeloma. Also up to 50% of autopsies done on these patients showed hepatic involvement. However, only rare cases have been reported of multiple myeloma leading clinically to non-obstructive cholestasis and progression into liver failure. Our patient was receiving treatment for myeloma and despite that his liver involvement was getting worse leading to severe cholestasis followed by progression into liver failure after the medications were stopped.

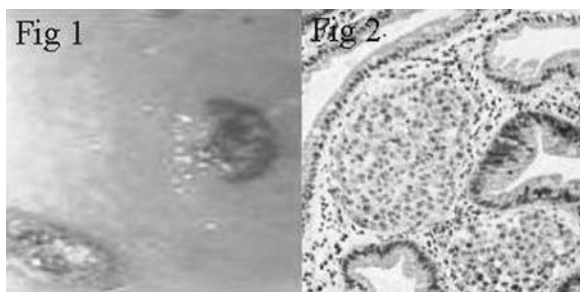
## 761

#### Metastatic Melanoma Presenting as Massive Upper Gastrointestinal Bleeding

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Symptomatic gastrointestinal involvement of malignant melanoma is seen in less than 5% of patients. We present a patient with massive upper gastrointestinal bleeding, found to have malignant melanoma as the cause.

A 66-year-old gentleman presented with epigastric pain, nausea, melena and coffee ground emesis. Past medical history included diabetes mellitus and hypertension, both well controlled with glyburide, enalapril and amlodipine. The patient denied any similar episodes in the past or any history of NSAID use. An upper endoscopy was performed revealing multiple black-pigmented lesions in the antrum and duodenum (Fig. 1). Biopsies were obtained. Pathology revealed duodenal mucosa with nests of cells in the lamina propria (Fig. 2). The cells demonstrated uniform nuclear features with occasional intra-nuclear cytoplasmic protrusions. Melanin pigmentation was identified. The findings were consistent with metastatic malignant melanoma. On further questioning, the patient reported an excision of a mole a year prior. Review of the pathology from that time revealed a melanoma that has been completely excised.[figure1]



Approximately 2–5% of patients with metastatic melanoma will have clinically significant GI symptoms, such as nausea, vomiting, abdominal pain, obstruction, and gastrointestinal bleeding. However, most patients are asymptomatic and have metastatic melanoma identified incidentally on endoscopy. Autopsy series of patients with advanced melanoma has shown that 60% have evidence of metastasis to the gastrointestinal tract. The most common locations for metastatic disease in the gastrointestinal tract include the small bowel (50%), colon (31.3%), and anorectum (25%). This case demonstrates that malignant melanoma to the stomach can be a cause of massive upper gastrointestinal bleeding.

762

#### Effectiveness of EUS in Liver Lesions of Unclear Etiology

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Endoscopic ultrasound (EUS) has assumed an important role in the diagnosis and staging of malignant GI tumors over the past few decades. EUS has widespread applications in the imaging of the GI tract, but has not been comprehensively studied in characterizing liver lesions. This case report describes the application of EUS in one such case.

**Case:** 24 yo male with hypoplastic kidneys s/p renal transplant  $\times$  2 (last being 7 years prior), chronic transplant nephropathy, and chronic pancreatitis presented with a 3-week history of epigastric pain. CT of abdomen without intravenous contrast (due to the patient's renal function) revealed a 3–4 cm mixed density lesion in the anterior segment of the right hepatic lobe which was biopsied under CT-guidance with aspiration of 10–15 ml of serosanguinous fluid. Biopsy cultures grew *Enterococcus* for which the patient was prescribed intravenous ampicillin/sulbactam for 6 weeks. The patient left the hospital AMA. Two weeks later, he returned to the hospital and underwent an MRI without contrast and a trans-abdominal ultrasound with equivocal findings. A repeat CT-guided biopsy was performed and revealed a bloody aspirate. EUS was performed and showed a 30  $\times$  40 mm vascular structure in the right lobe of the liver with turbulent flow with a doppler characteristic of an arterial structure, consistent with an arterio-venous malformation. Four weeks later, the patient presented with sharp epigastric pain, melena, and icterus. Labs revealed a total bilirubin of 22.5 mg/dL and a significant decrease in hemoglobin (10 to 5.9 g/dL). An EGD revealed esophagitis. Side-view endoscopy (duodenoscopy) demonstrated blood-tinged bile from the major papilla. Contrast injection revealed blood clots obstructing the CBD, which was cleared and stented with a 10-Fr 10 cm plastic stent. The cause of the upper GI bleed was determined to be hemobilia.

**Conclusions:** This case report suggests the use of EUS as the imaging modality of choice for the liver prior to any therapeutic endeavor for patients who have contraindications for radiological contrast. Although scant information is available on the use of EUS as a primary imaging modality in cases such as these, this report suggests EUS may serve an important role in identifying liver lesions and preventing potential iatrogenic complications.

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#### Endoscopic Mucosal Resection of H. Pylori Negative Esophageal MALT Lymphoma

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**Introduction:** MALT lymphoma is a cancer of gastrointestinal mucosa associated with H. Pylori infection. Less than 1% of MALT lymphoma occur in the esophagus. Esophageal MALT lymphoma has previously been treated with radiation therapy. We describe a case of Endoscopic Mucosal Resection as therapy for the treatment of esophageal MALT lymphoma confined to the mucosa.

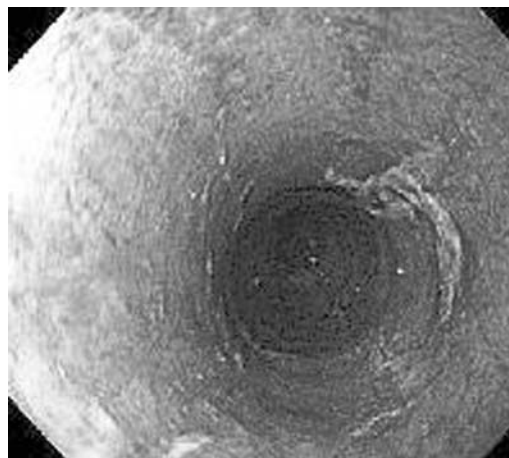
**Case:** A 38 year old female presented with 3 months of GERD symptoms despite treatment with a variety of medications. She denied hematemesis, melena, hematochezia or unintended weight loss. She denied alcohol or tobacco use. Her family history is significant for a father with colon polyps. Physical exam was unremarkable. Laboratory analysis: WBC 8, HCT 43, Plts 275, K 4.0, Cr 0.7, LFT normal. H. Pylori IgG Negative. An EGD was performed that demonstrated a 4.4 mm  $\times$  1.8 mm nodule 4 cm above the GE junction. Biopsies of the nodule demonstrated lymphoma. Gastric biopsies demonstrated no evidence of H. Pylori or malignancy. EUS demonstrated a hypoechoic lesion with 2 mm of depth localized to the mucosa. CT scan showed no evidence of lymphadenopathy or other disease. The nodule was removed with an EMR technique. It was first raised with 10 cc of normal saline. An oblique 16 mm hard EMR cap was attached to a single channel therapeutic endoscope and the nodule was removed using a snare. Histopathology showed extranodal monoclonal kappa restricted marginal cell lymphoma with normal surrounding mucosa. Immunohistochemistry demonstrated: LCA+/CD20+/CD79a+ Bcl-2 staining demonstrated residual reactive germinal center.

**Discussion:** Extranodal MALT lymphomas arise in mucosal organs of the gastrointestinal tract, usually in the stomach and colon. H. Pylori infection is the usual underlying etiology of MALT lymphoma in the stomach and eradication of H. Pylori is the initial treatment of choice for gastric MALT lymphoma. This patient demonstrated no evidence of H. Pylori infection on either gastric biopsy or serology. MALT lymphoma in the esophagus is very rare. MALT lymphomas are confined to the primary site and tend to disseminate slowly. There have been two previously documented cases of MALT lymphoma arising in the esophagus. In these reports EMR has been demonstrated to be an effective technique to remove MALT lymphoma that has not invaded the muscularis. Complete removal of esophageal MALT lymphoma with EMR precludes further treatment with radiation therapy.

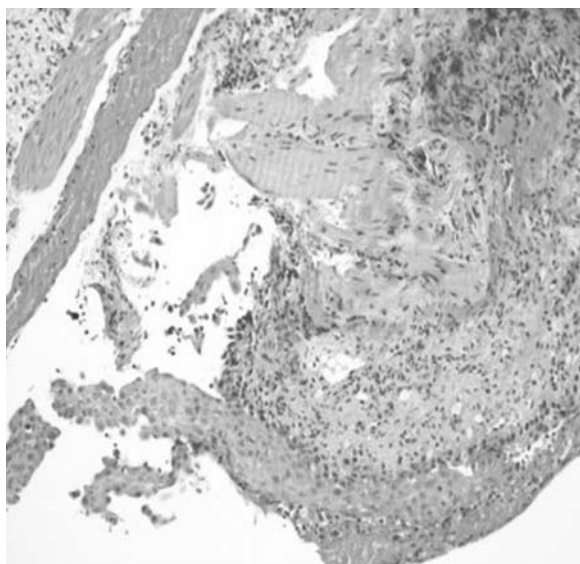
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#### An Unusual Presentation of Pemphigus Vulgaris

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Pemphigus vulgaris (PV) is a potentially life-threatening autoimmune disease targeting skin and mucous membranes. The disease is characterized by disruption of adhesion of the keratinocytes termed *acantholysis* <sup>(1,2)</sup>. Although oral and pharyngeal involvement is very common, esophageal involvement is reported to be less common and is mostly confined to case reports and case series. Esophageal involvement usually manifests as odynophagia and dysphagia, while hematemesis is rare. Here, we report a case of PV involving the esophagus and presenting as hematemesis, requiring endoscopic intervention for hemostasis.[figure1][figure2]



765

#### Uveal Melanoma with Hepatic Metastases: A Case Report

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A 44 year-old female presented with a one-week history of RUQ abdominal pain without nausea, change in bowel habits or weight loss. PMHx was unremarkable and FHx was significant for colorectal cancer in her father who died at age 50 and a brother with multiple polyps at age 40. There was moderate RUQ tenderness and rectal exam showed hemoccult positive brown stool. Labs: Hgb:8.8, Hct:27.6, MCV:65, AST:80, ALT:128, ALK:101, T.Bili:0.1.CT ABD: multiple hypodense hepatic lesions suspicious for metastatic disease. Based on these findings, our initial differential diagnosis included colorectal cancer with hepatic metastases given the patient's presentation of hemoccult positive stool with microcytic anemia in the setting of a family history of colorectal cancer and colonic polyps in two first degree relatives. Additional studies revealed normal tumor markers and an unrevealing EGD and colonoscopy. As a result, our revised differential for hepatic metastases of an unknown primary included malignancies of the lung, breast, kidney, ovary, thyroid and lymphatics. Liver biopsy was performed and stained positive for HMB-45, MART-1 and S-100 consistent with metastatic melanoma. Additional patient history revealed a significant history of sun exposure, irregular nevi and as a result, the primary site of melanoma was assumed to be cutaneous in origin. However, during this time the patient was also evaluated by her ophthalmologist for progressively worsening visual acuity. On exam, the patient was determined to have a lesion consistent with ocular melanoma of the iris. The patient was subsequently treated with intra-hepatic chemotherapy for uveal melanoma with hepatic metastases without any improvement and died 67 days after initial presentation.

Malignant melanoma of the uveal tract (iris, ciliary body, choroid) is rare and the most common non-cutaneous melanoma in adults. The liver is the predominant organ involved in up to 95% of cases with metastatic disease. Approximately 60% of patients with metastases are asymptomatic and 30% may have normal LFT's. Although liver involvement tends to be the first manifestation of metastatic disease, the role of systemic screening is controversial because of the paucity effective therapy. Metastatic uveal melanoma is very aggressive with a poor prognosis and a median survival less than six months. This case illustrates the aggressive nature of metastatic uveal melanoma and highlights the importance of including melanoma in the differential for hepatic metastases.

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#### Conservative Management of Inadvertent Colon Penetration during Percutaneous Gastrostomy Tube Placement

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Percutaneous endoscopic gastrostomy (PEG) is the preferred method for long-term enteral nutrition access. Major complications are infrequent. One complication often requiring surgery is inadvertent colonic perforation. We report 2 cases of PEG-related colon injury with benign courses that did not require surgery.

**Case 1:** 57 year-old male, with dysphagia from an intracranial hemorrhage, was consulted for PEG placement. His only relative contraindication for PEG was a prior partial gastrectomy for peptic ulcer disease. A PEG was easily placed after seeing clear transillumination and distinct finger indentation in the gastric wall; the tube placement was endoscopically confirmed. Follow-up exam on days 1 and 3 were normal. Eleven days later, the patient had feculent material in the PEG tube. At this time, the abdominal exam was benign. WBC was 15.1 and KUB showed the PEG traversing the colon into the stomach. Follow-up abdominal CT revealed the PEG bumper was in the transverse colon. No pneumoperitoneum, abscess, or gastrocolic fistula was seen. The PEG was removed 17 days after placement and subsequent exams and labs were normal. The PEG tract closed without incident and the patient expired 1.5 months later from pneumonia.

**Case 2:** 80 year-old male was evaluated for PEG placement to prevent recurrent aspiration pneumonia from Parkinson's related dysphagia. There were no contraindications for the PEG. The procedure was uncomplicated and the follow-up exam was benign. The patient was discharged home tolerating tube feedings. He returned to the emergency room 40 days later after inadvertently pulling out the PEG. A replacement tube was inserted, but could not be advanced. A Gastrografin tube-study showed contrast filling the colon at the splenic flexure, without reflux into the stomach. At this point, the abdominal exam was benign. There was no leukocytosis. The PEG was removed and the patient was observed. No problems occurred and the tract closed spontaneously.

These cases illustrate the indolent course of transverse colon penetration during PEG placement. Although there is a risk for peritonitis, many cases may be silent unless the PEG becomes dislodged. Given this observation, one could surmise that PEG-related colon injury is more frequent than previously reported. However, in light of these benign outcomes, conservative management may be considered if no acute findings exist.

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#### Acute Myelomonocytic Leukemia Manifesting as Ileus

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**Introduction:** Acute Myelomonocytic Leukemia (AMML) is a malignancy of myeloid stem cells with monocytoid differentiation which predominantly involves the marrow and blood. It often involves the gingiva but can also occasionally involve other extramedullary sites such as lymph nodes, mediastinum, uterus and rarely the small intestine. We present a rare case of a patient with known but untreated, chronic myelomonocytic leukemia (CMML) which converted to AMML. The patient was subsequently found to have motility impairment due to leukemic infiltration of the small bowel.

**Case:** Patient was a 70 yr. old male with a one year history of asymptomatic CMML which converted to AMML. He presented to the hospital with complaints of abdominal distention and diffuse constant abdominal pain. The clinical presentation and imaging studies supported a diagnosis of small bowel obstruction vs ileus. Subsequent endoscopic intervention demonstrated no evidence of gross obstruction, with small bowel biopsies consistent with leukemic infiltration of the bowel wall.

**Discussion:** Extramedullary involvement of the gastrointestinal tract by myeloid leukemia leading to dysfunction is a rare phenomena. In our patient there was conversion of CMML to AMML, a more aggressive myeloid leukemia with predilection to tissue infiltration of sites such as the small intestine. Lymphoid leukemic involvement of the GI tract is more common and often involves the ileum, stomach and proximal colon. There is a wide variety of clinical presentations ranging from appendicitis, intussusception to small bowel obstruction. The literature is sparse with reports of myeloid involvement. The pathophysiology behind this patient's symptoms is thought to be secondary to motility dysfunction from leukemic blast infiltration of the neuromuscular layer of the small bowel leading to an ileus. Leukemic involvement of the gastrointestinal tract should be considered in a patient with leukemia who presents with unusual gastrointestinal symptoms.

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#### **Delivery of Agile Patency Capsule Using an Endoscopic Delivery Device**

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The Agile Patency Capsule is an ingestible dissolvable non-video capsule, which has been in use in U.S since 2006. It is indicated in patients with suspected intestinal obstruction prior to ingestion of the Pillcam. Ingestion of the Agile Patency Capsule is contraindicated in patients with swallowing disorders. Theoretically, this limitation could be overcome by passing the capsule endoscopically, using a capsule delivery device (US Endoscopy). Because of the circumference and the consistency (barium makeup) of the Patency Capsule there are concerns about whether the delivery device would be functional. To report our clinical experience with successful delivery of the Agile Patency Capsule using the capsule delivery device and the difficulties encountered in the deployment of the capsule.

Two patients underwent attempted deployment into the small bowel because of gastric retention. Both patients had a suspicion of partial small bowel obstruction. Prior to intubation, the delivery device was passed through the biopsy channel of the endoscope and the Agile Capsule was inserted into the device. The endoscope was then passed through the mouth under direct visualization and advanced into the 2nd portion of the duodenum.

One deployed without difficulty. In the second patient, upon releasing the capsule, the deployment cable of the device lodged in the distal end of the Agile Capsule, preventing the release of the capsule. Release of the capsule was quickly achieved by simply jiggling the endoscope.

This is the first reported experience utilizing the delivery device for the Agile Patency Capsule. The Agile Capsule's make-up and size are different from the Pillcam but still acceptable for deployment. Endoscopists should be aware of the potential for the cable to penetrate and lodge within the capsule.

769

#### **Sclerosing Cholangitis and B-Cell Lymphoma in a Patient with Chronic Hepatitis C**

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**Introduction:** Diffuse large B-cell lymphoma (DLCL) commonly presents in the seventh decade of life and spreads aggressively to extra-nodal tissues. DLCL, when responding to therapy, has a long-term survival rate of 50%. The complications of DLCL are multifold. A literature review has revealed only one report of sclerosing cholangitis (SC) as a complication of B-cell lymphoma. In contrast, a recent meta-analysis has described an association between hepatitis C virus (HCV) infection and DLCL. We present a patient with chronic HCV infection, who was diagnosed with DLCL and secondary SC.

**Case Report:** A 45-year-old Caucasian female with a six-year history of HCV infection, genotype 1b, presented with vague acute abdominal pain. Physical examination revealed jaundice, pruritus and choloria. The patient experienced mild dyspnea, but denied fevers or sweats. Laboratory analysis showed a total bilirubin (TB) of 4.5 mg/dL, with direct predominance, alkaline phosphatase (AP) of 272 mg/dL and AST of 59 mg/dL. An abdominal CT scan showed scattered, hypodense hepatic foci, suggestive of a diffuse, infiltrative process. There was extensive abdominal lymphadenopathy and mild ascites. A CT-guided liver biopsy showed DLCL. Due to progressive cholestasis (TB = 22.5 mg/dL and AP = 330 mg/dL) an ERCP was performed, showing several areas of narrowing interspersed with dilations in the intra-hepatic bile ducts, consistent with diffuse SC. No dominant stricture was seen; therefore, endoscopic intervention was not performed. Following chemotherapy, the patient achieved an excellent response with resolution of clinical, radiographic and laboratory abnormalities.

**Discussion and Conclusion:** Secondary SC refers to a radiological and clinical syndrome that is similar to primary SC but results from a known pathogenesis or injury, including obstructive, toxic, ischemic, and neoplastic causes. In this report, we describe a patient with chronic HCV infection who developed DLCL complicated by secondary SC. In conclusion, secondary SC should be suspected with unexplained cholestasis complicating DLCL.

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#### **Oriental Hepatolithiasis in an African Patient Presenting with Subfulminant Hepatic Failure**

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**Background:** Oriental hepatolithiasis, also known as recurrent pyogenic cholangitis, is a disease characterized by intrahepatic pigment stone formation, dilatation and stricturing of biliary tree. Patients usually present with recurrent episodes of cholangitis leading to chronic biliary obstruction, liver abscess, liver atrophy and eventually secondary biliary cirrhosis. To our knowledge, there are no case reports of Oriental hepatolithiasis in African patients presenting with subfulminant hepatic failure.

**Methods:** We describe a 28 year old African female from Nigeria who presented with a 1 month history of progressive scleral icterus, abdominal distention and lower extremity edema. Liver enzymes were elevated with Bilirubin: 20.8 mg/dl, Alkaline Phosphatase: 514 U/l, AST-297 U/l, ALT-104 U/l, INR-2.03. Workup for chronic liver disease showed ANA>1:160, Anti SM(-), Anti LKM1(-). MRI/MRCP showed cirrhotic liver with moderate intrahepatic biliary dilatation. Patient was given a trial of steroids therapy for possible Auto-immune hepatitis without any clinical response. Transjugular liver biopsy was non-diagnostic. Patient underwent OLT for hepatic failure within 2 months of her presentation. Histopathology of explanted liver showed mixed nodular cirrhosis and diffuse severe intrahepatic bile



sludging and hepatolithiasis, marked cholangiolar proliferation, foamy cells and distended bile ducts suggestive of "oriental hepatolithiasis".

**Conclusion:** Although many patients with Oriental hepatolithiasis present with a chronic progressive course, our patient presented with subfulminant hepatic failure. Liver transplantation should be considered as an additional therapeutic modality in these patients.

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#### Wireless Capsule Endoscopy in a Patient with Intermittent Obstructive Symptoms – A New Indication

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**Background & Aims:** Wireless capsule endoscopy (WCE) has emerged as a valuable tool for the diagnosis of small intestinal pathology. A previous relative contraindication to WCE was administration of the capsule device to patients with a history of obstructive symptoms. The aim of this report is to describe a patient with recurrent small bowel obstruction in whom no intra-luminal etiology could be found by standard imaging and endoscopic techniques, but was discovered by WCE.

**Case Presentation:** A seventy year-old man with history of chronic nonsteroidal anti-inflammatory medication (NSAID) use, recurrent small intestinal obstruction, and iron deficiency anemia had previously undergone seven abdominal surgeries with exploration and lysis of adhesions, each with only transient relief of symptoms. Computer tomogram of the abdomen showed distended loops of small bowel consistent with partial small bowel obstruction. However, small bowel series showed no abnormality of mucosal pattern or contour of the jejunum and ileum. Transit time was also normal at 2 hours. WCE was performed due to persistent symptoms. The WCE examination was incomplete with retention of the capsule in the distal jejunum or ileum. Review of the images from the wireless capsule device revealed an endoluminal stricture in the distal small intestine and associated clean-based ulcer with two small, nonbleeding erosions believed secondary to chronic use of NSAIDs. Delayed abdominal plain films fifty-seven days after WCE demonstrated the capsule retained in the distal ileum. A laparoscopic small bowel resection with end-to-end anastomosis was performed to remove the retained capsule and resect the area of stricturing. Gross specimens showed small intestinal luminal narrowing proximal and distal to the capsule. Pathology revealed luminal narrowing with focal areas of erosion consistent with NSAID diaphragms. The patient is now symptom free.

**Conclusions:** This report lends credence to a new indication for wireless capsule endoscopy in order to identify occult sources of bowel obstruction while simultaneously visualizing these areas to discover endoscopic pathology.

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#### Giant Hyperplastic Gastric Polyps: Precursor Lesions to Adenocarcinoma?

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**Purpose:** Genetic analyses and histopathological studies in the past have proposed a possible progression of both Focal Foveolar Hyperplasia (FFH) and Hyperplastic polyps (HP) to adenocarcinoma.

**Methods:** In this case report we present a 31 y/o male who was followed for a period of 12 years secondary to intractable GERD. Initially he was managed medically with proton pump inhibitors, but despite prolonged treatment there was only partial relief in his symptoms. For further investigation an upper endoscopy was performed which showed FFH in the antral region of the stomach and the decision was made to continue medical management. Ten years after the initial presentation an endoscopy was repeated due to

intractable vomiting, weight loss, and dyspepsia. Endoscopy showed multiple gastric polyps, the most prominent of which measured about 12 cm in diameter arising from the initial site of FFH.

The decision was made to remove the giant polyp due to the fact that his symptoms were attributed to the overall size of the polyp. The biopsy of the giant HP showed fragments of tubular adenoma with high-grade glandular dysplasia in the background of mucosal hyperplasia, and without any signs of invasive malignancy. The patient underwent partial gastrectomy in order to completely remove the polyp, after which he had partial relief of his symptoms.

After a period of 1 year he presented again with severe dyspepsia and early satiety. Repeat endoscopy demonstrated that the entire gastric mucosal surface was carpeted by polypoid structures ranging from barely visible up to 11 cm in diameter. Random biopsy specimens confirmed high-grade dysplasia. Due to the fact that random biopsy may have missed areas of invasive malignancy, a decision was made to perform a total gastrectomy. During the operation the stomach was found to be 90 cm × 60 cm with dilated and thickened walls, secondary to the presence of numerous polyps. The wall thickening was localized to the stomach and did not extend beyond the GE junction or the pylorus. Pathology specimens from the total gastrectomy showed focal high-grade dysplasia with foci suggestive of intramucosal adenocarcinoma.

**Results:** The above case report highlights a possible association between both FFH and hyperplastic polyps and their progression to invasive malignancy. The rapid transformation of the hyperplastic polyps in our case report suggests a need for earlier and more aggressive interventions in patients with these findings.

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#### Therapeutic Success of Rifaximin in the Setting of Clostridium Difficile Diarrhea Refractory to Metronidazole and Vancomycin: Case Report

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**Purpose:** Diarrhea following the use of antibiotics is an infrequent complication. We report a case of a 42 year-old Caucasian male that suffered from chronic diarrhea following a two-week course of fluoroquinolone therapy for pneumonia. The patient's complaints included bloating and at least 10 episodes of watery diarrhea per day. Stool studies were positive for Clostridium difficile and pseudomembranes were found on endoscopy. The acute diarrhea was treated with a two-week course of metronidazole. Although the diarrhea resolved while on therapy, it recurred within days of stopping the medication. This sequence of events took place for a second time as the patient suffered a recurrence following another two-week regimen of metronidazole. Subsequently, the patient was treated with a two-week course of vancomycin, during which the diarrhea resolved. However, following discontinuation of the vancomycin treatment, the diarrhea recurred once again. During this last episode of recurrent diarrhea, which lasted 10 days, the patient developed signs of dehydration and renal dysfunction. He was admitted for intravenous fluid replacement and treated with rifaximin 400 mg orally three times per day. The diarrhea and associated symptoms resolved within 24 hours and the patient was discharged home to complete a 4 week regimen of rifaximin. Three months after completion of therapy, the diarrhea remained suppressed. There are few case reports demonstrating the role of rifaximin in the treatment of C. difficile colitis, but its role in refractory cases is unknown. This report describes a dramatic clinical response to rifaximin in the setting of refractory Clostridium difficile diarrhea and demonstrates this regimen as an alternative treatment.

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#### Celiac Disease and Chronic Infectious Enteritis

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**Purpose:** Gliadins are polypeptides found in wheat, rye, oats, barley, and other grains and glutens. They are toxic to the intestinal mucos in susceptible individuals. The purpose of this report is to demonstrate the presence of salivary antibodies to gliadin (GliadinAb, SIgA) in patients with chronic infectious enteritis.

**Methods:** Two hundred thirty four (234) patients (ave. age 33 yrs., M/F 102:132) found to have infectious enteritis with one or more pathogens (*Blastocystis hominis*, *Giardia lamblia*, *Cryptosporidium parvum*, *Amoeba histolytica*, *Helicobacter pylori*) were simultaneously tested for GliadinAb-SIgA (Diagnos-Techs, Inc.).

**Results:** The mean GliadinAbSIgA in the 234 cases of chronic infectious enteritis was >20 U/ml. (normal <13 U/ml., borderline 13–15 U/ml., positive >15 U/ml.).

**Conclusion:** Patients with chronic infectious enteritis have elevated levels of GliadinAbSIgA. This suggests these individuals are rendered susceptible to Celiac Disease on this basis; a cause and effect relationship. Further studies to determine the effect of successful treatment of chronic infectious enteritis on production of GliadinAbSIgA are warranted.

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#### Peroral Cholecystoscopy-Directed Electrohydraulic Lithotripsy of Symptomatic Cholecystolithiasis in Poor Surgical Candidates

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**Purpose:** Laparoscopic cholecystectomy is the treatment of choice for symptomatic gallstones, but not for those who are poor surgical candidates. Cholecystoscopy-directed electrohydraulic lithotripsy (EHL) using a “baby scope” passed through a side-viewing duodenoscope is effective for treating choledocholithiasis. However, this technique has not been reported for the treatment of symptomatic cholecystolithiasis in patients unable to undergo surgery. This report describes two cases that demonstrate, for the first time, the feasibility of peroral cholecystoscopy-directed EHL (PC-EHL) for treating symptomatic cholecystolithiasis in non-surgical candidates.

**Case 1:** 78 yo female with severe COPD and cholecystostomy tube for recurrent cholecystitis presented with symptomatic cholelithiasis. A laparoscopic cholecystectomy was attempted and aborted due to severe gallbladder inflammation. The patient was a poor surgical candidate based on poor pulmonary status and prior failed surgery. She underwent a PC-EHL of a 3 cm gallstone and multiple smaller gallstones. Subsequently, a 10-Fr, 10 cm cystic duct stent and a 7-Fr CBD stent were placed. After 12 weeks, a repeat ERC showed only fragments of the stones which were washed and removed. A 7-Fr double pigtail gallbladder stent was placed. With follow-up, she has experienced an uneventful recovery and a marked improvement in her symptoms.

**Case 2:** 65 yo male with ischemic cardiomyopathy (NYHA class IV) and recurrent cholangitis s/p cholecystostomy and gallbladder stenting presented with symptomatic cholelithiasis. The patient was a poor surgical candidate based on poor cardiac status. He underwent PC-EHL of a 5 cm gallbladder stone. Subsequently, a 10-Fr double pigtail stent was placed into the gallbladder. After 2 weeks, a repeat ERC demonstrated a 2 cm fragment of the prior stone. A 10-Fr, 10 cm and a 7-Fr, 10 cm double pigtail stents were placed into the gallbladder. The patient is scheduled for cholangioscopy with repeat EHL. With follow-up, he has experienced an uneventful recovery and a marked improvement in his symptoms.

**Conclusion:** These cases represent the first successful demonstration of PC-EHL in the management of symptomatic cholecystolithiasis. This novel technique offers an endoscopic approach to managing patients with symptomatic cholecystolithiasis who are not surgical candidates.

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#### Adenocarcinoma at the Colostomy Site in a Patient Presenting for Ulcerative Colitis Dysplasia Surveillance

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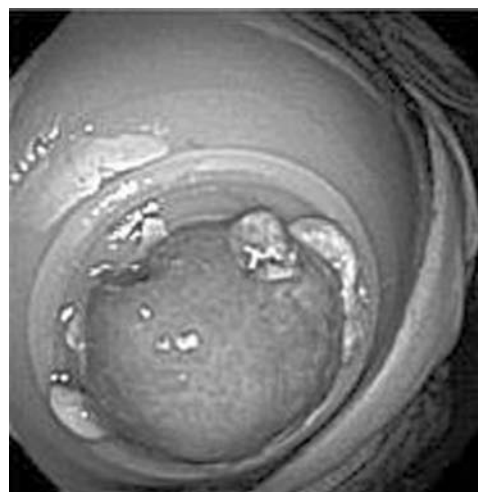
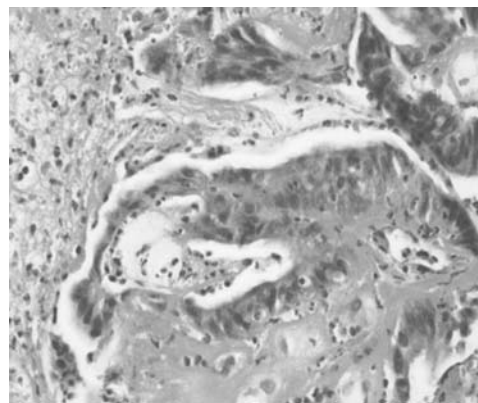
**Purpose:** A 60 year-old man with 26 year history of ulcerative colitis presented for routine surveillance colonoscopy. He underwent a partial colectomy at an outside hospital in the remote past with remaining descending colostomy and rectal stump. His last colonoscopy was 2 years prior with no dysplasia on biopsy. Follow-up colonoscopy was performed which revealed quiescent colitis from the cecum to the descending colostomy. However, upon closer inspection of the stoma, a 5 mm lesion, thought to be an inflammatory nodule, was found on the periphery of the stoma. A biopsy was taken, which showed a moderately differentiated adenocarcinoma. He subsequently was seen by general surgery and underwent a total proctocolectomy with end ileostomy.

**Discussion:** Patients who have had ulcerative colitis for 8–10 years should have a surveillance colonoscopy with a minimum of 32 biopsy specimens from the cecum to the rectum every 1–2 years. Primary adenocarcinoma arising from a colostomy site is very rare and has been reported in the literature only a few times. This case demonstrates the importance of careful visual inspection of the stoma during surveillance colonoscopy; and recognition that the stoma *itself* should be included in dysplasia surveillance.

#### REFERENCE

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[figure1][figure2]



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### Chronic Mesenteric Ischemia Presenting as *Helicobacter pylori*-Negative Duodenal and Gastric Ulcers. Case Report and Literature Review

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**Purpose:** Vascular insufficiency syndromes involving arterial supply can rarely present with peptic ulceration that is unrelated to *H. Pylori* infection or NSAID use. Gastric ischemia is extremely rare, given the rich arterial supply to the stomach.

We are reporting an 80-year-old female who presented to our hospital with approximately 10 week history of postprandial nausea, abdominal discomfort and occasional vomiting. She described the pain as dull band-like discomfort in the periumbilical region. She denied any diarrhea, constipation, melena or hematochezia. Esophagogastroduodenoscopy three weeks prior to admission revealed multiple gastric and duodenal ulcers. *H. Pylori* was negative. Colonoscopy revealed right-sided diverticulosis.

Her pain was progressively getting worse without improvement with the use of a proton-pump inhibitor. She lost 15 pounds over 3 months and had multiple visits to the emergency department. The patient had history of hypertension, hyperlipidemia and pelvic vein thrombosis. She had a history of tobacco smoking and did not consume alcohol or illicit drugs. Her medications included rabeprazole, Lipitor, Coumadin and metoprolol. She was recently taken off her Alendronate. She denied any use of corticosteroids or NSAIDs.

No icterus was present. The abdomen was soft, nondistended and had normal bowel sounds. There was tenderness in the periumbilical and epigastric region to palpation without palpable masses or rebound tenderness. The patient had guaiac-negative stool. Laboratory studies revealed normal lipase, amylase and liver function tests. Gastrin concentration was 376 pg per milliliter (normal range 0–110). Abdominal CT was unremarkable. Abdominal Doppler, Abdominal MRA and later traditional angiography demonstrated occlusion of the proximal aspects of the celiac artery and superior mesenteric arteries. The patient underwent repair of her celiac and superior mesenteric axis by antegrade bypass. She tolerated the surgery well and was discharged in a stable condition.

Ischemic peptic ulcer disease is seldom diagnosed. Certainly, the reconstitution of the patient's well-being after revascularization suggest that this very unusual combination was responsible for her clinical picture and the endoscopic findings.

**Conclusion:** This case suggests that ischemia as an etiology for peptic ulcer disease should be considered in *H. Pylori* negative ulcers even in gastric ulcers.

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### Nitazoxanide and Treatment of *Helicobacter pylori*

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**Purpose:** Out of hundreds of patients seen in consultation for chronic gastrointestinal infection/parasitosis 212 were found to have *H. pylori* infection by salivary testing. The purpose of this report is to present a novel diagnostic and therapeutic strategy for *H. pylori* utilizing a single therapeutic agent, Nitazoxanide, along with pre- and post-diagnostic monitoring utilizing salivary antibody testing (HpSIgG).

**Methods:** Seventy nine (79) patients (mean age 49 yr., M/F = 30:49) with *H. pylori* infection detected by HpSIgG (Diagnos-Techs, Inc.) were prescribed one drug, Nitazoxanide (1 gram, PO, BID, for two weeks). Patients were not allowed to take any acid inhibiting agents of any sort. Carafate was permitted on a PRN basis for relief of symptoms. Post therapeutic testing with HpSIgG was obtained (2–4 months) in all cases.

**Results:** Of the seventy nine patients treated with Nitazoxanide alone post therapeutic HpSIgG testing indicated eradication of infection in seventy three (73/79; 92%).

**Conclusion:** Nitazoxanide is a very effective one drug therapy for *H. pylori*. An added advantage is that it is also simultaneously effective against a host of concomitant enteric infectious agents and parasites. Salivary testing for *H. pylori* is a convenient and non-invasive method for pre- and post-therapeutic detection of *H. pylori* infection.

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### The GIST (Gastrointestinal Stromal Tumor) of the Gastroesophageal Junction (GEJ)

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**Purpose:** The histology of primary GEJ tumors is most often adenocarcinoma, and less often, squamous cell carcinoma. Rarely, GEJ tumors are due to other primary epithelial malignancies (small cell carcinoma, melanoma or carcinosarcoma) or nonepithelial neoplasms (lymphoma, sarcoma such as GIST, or other mesenchymal tumors). Metastases to the GEJ can also rarely occur. We describe a patient with a GIST of the GEJ.

**Case:** A 75-year-old man was evaluated for iron deficiency anemia and stools that were positive for occult blood. He noted dysphagia and early satiety. An upper endoscopy showed a submucosal mass at the GEJ extending into the gastric cardia. The mass measured 10 cm. There was central ulceration with a necrotic tumor cavity, best seen on retroflexion. Biopsies of the ulcerated area showed a spindle cell neoplasm which stained positive for CD117 (c-kit), confirming a GIST. Computed tomography and positron emission tomography confirmed the GEJ mass, while no metastases were detected. He underwent a trans-thoracic open partial esophagogastrectomy. Pathology confirmed a high grade GIST of the GEJ, with negative nodes. There has been no recurrence as of 9 months of follow up.

**Discussion:** Our patient had a GIST of the GEJ. It most likely arose from the gastric cardia, based on location of the tumor's epicenter and pathological evaluation. The vast majority of esophageal primary mesenchymal tumors are leiomyomas. In contrast, the most frequent site of gastrointestinal GISTs is the stomach, most commonly the gastric fundus. These tumors, including those involving the GEJ, are amenable to laparoscopic resection. The gist of this patient's GEJ is that GISTs should be included in the differential diagnosis of GEJ neoplasms.

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### Pneumatosis Intestinalis of Small Bowel Due to Acute Pancreatitis Induced Ileus

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**Purpose:** Pneumatosis intestinalis (PI) is a condition characterized by the presence of gas within the wall of the small or large intestine. Common conditions responsible for pneumatosis intestinalis include inflammatory bowel disease, infectious gastroenteritis, intestinal obstruction, chronic obstructive pulmonary disease, and AIDS. In rare instances, PI may portend a life threatening intra-abdominal catastrophe.

**Methods:** A 52 year-old African American male with history of HIV on retroviral therapy, hepatitis C, hypertension, alcohol abuse, and a ventral hernia repaired six months prior was admitted for mid epigastric pain associated with nausea and vomiting. On physical exam, the patient had a reducible ventral hernia, hypoactive bowel sounds, epigastric tenderness, and voluntary guarding without rebound or rigidity. Laboratory studies revealed amylase 1065, and lipase 1130. An abdominal obstructive series revealed moderate gaseous distension of small bowel loops and right colon. A CT scan of the abdomen was significant for markedly distended stomach and small bowel loops with pneumatosis in one of the dilated loops of the small bowel in the left lower quadrant; the large bowel was also partially distended. The liver, spleen, gallbladder, and pancreas were unremarkable. An ultrasound of the

abdomen revealed mildly prominent intrahepatic biliary ducts. The common bile duct was 8 mm in diameter. The patient was treated conservatively with subsequent improvement.

**Results:** [figure1]



**Conclusion:** We report a case of PI due to acute pancreatitis-induced ileus. For patients who are asymptomatic or minimally symptomatic, the recommended management includes hyperbaric oxygen, antibiotics, elemental diet, and treatment of the underlying cause. Intramural gas cysts usually resolve spontaneously.

## 781

### Profound Gastroparesis Presenting with Isolated Intrahepatic Amyloidosis

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**Purpose:** Amyloidosis of the gastrointestinal tract usually results in either mucosal or neuromuscular infiltration. Mucosal infiltration causes mucosal friability, erosions, ulcerations or thickening of the the intestinal wall, which in turn causes nausea, vomiting, gastrointestinal bleeding, and malabsorption. Neuromuscular infiltration may cause gastrointestinal motility disorders. We present a patient with profound gastroparesis found to have intrahepatic amyloidosis as the cause.

**Methods:** A 51 year old male presented with complaints of nausea, vomiting, and epigastric pain. Due to early satiety, there had been a significant weight loss, but no fever, diarrhea or constipation. The patient's past medical history was significant for schizophrenia and glaucoma. His medications included risperidone, clozapine, pilocarpine, metoclopramide, timolol and megestrol. Physical examination revealed a catatonic male of moderate build

with diffuse abdominal distension and tenderness. No hepatomegaly was noted. Rectal examination was normal and fecal occult blood test negative. An abdominal radiograph showed massive gastric distension. A computer assisted tomography scan of the abdomen and pelvis revealed a grossly distended stomach with an abrupt tapering at the duodenum, no obvious mass. Prior to endoscopic evaluation, an Ewald tube was inserted with removal of feculent material from the stomach. Endoscopic evaluation to the distal duodenum revealed irregular large ulcers in the stomach and a normal duodenum. The patient had a complicated hospital course with respiratory distress, intubation, and sepsis. Progressive gastric dilatation resulted in ischemic ulceration and perforation of the stomach. Exploratory laparotomy was performed. A wedge resection of the gangrenous, perforated area of the stomach was performed. Pathology showed gastric mucosa with extensive necrosis, transmural inflammation and perforation. Extensive granulation tissue with diffuse amyloid in the perigastric fat.

**Conclusion:** This case represents the first case of gastrointestinal intra-peritoneal amyloidosis causing gastroparesis. Our case is unique in that the site of the amyloid deposit was found in perigastric fat rather than in the mucosa, vascular endothelium, or the nerve tissue. Based on our findings, in patients presenting with idiopathic gastroparesis, a full thickness biopsy should be performed to rule out amyloidosis.

## 782

### Sinusoidal Occlusion Syndrome Following Exposure to Gemtuzumab: Unsuccessful Treatment with Defibrotide

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**Purpose:** Sinusoidal occlusion syndrome (SOS) is a rare, life-threatening disorder characterized by abdominal distention, weight gain, tender hepatomegaly, ascites, and elevated aspartate aminotransferase (AST) and creatinine (Cr) concentrations. Ultrasonography (US) demonstrates patent portal and hepatic venous circulations. SOS arises most commonly in the setting of bone marrow transplantation (BMT). Gemtuzumab, an anti-CD33 monoclonal antibody, is a new agent for the management of relapsed acute myeloid leukemia (AML). Abnormal liver tests occur in 1/3 of gemtuzumab-treated patients, but only 1–2% have documented SOS.

A 24 year-old man, diagnosed with AML 13 months after receiving chemotherapy for a mediastinal germ cell malignancy failed to respond to initial protocol chemotherapy with amonafide, cytarabine and mitoxantrone. Salvage chemotherapy with gemtuzumab was initiated in standard dose and schedule. Five days after first exposure to gemtuzumab the patient began gaining weight, and by day 9 his weight gain was 4 kg. His abdomen was distended and uncomfortable, and he required oxygen for dyspnea. Laboratory studies were as follows: AST 6733 IU/L (normal range [NR]: 10–60), alkaline phosphatase 162 IU/L (NR: 30–135), prothrombin time 17.7 s (NR: 11.1–13), total bilirubin 1.9 mg% (NR: 0.2–1.2) and Cr 5.9 mg% (NR: 0.4–1.4). US scan confirmed the presence of splenomegaly and ascites; the hepatic and portal vein branches were patent. However, the direction of flow in the latter was reversed. Both the vena cava and hepatic artery were patent. Relevant acute viral, metabolic and immune forms of liver disease were excluded on the basis of appropriate serologic studies. Given the symptom complex, compassionate approval was sought for use of the non FDA-approved drug, defibrotide. However, despite this intervention, continuous veno-veno hemodialysis, and further antimicrobial therapy, the patient developed acute liver failure and died 26 days after first gemtuzumab exposure.

This man's clinical, laboratory and US findings met diagnostic criteria for SOS. While experience with SOS in the BMT setting is well recorded, other etiologies are rarely recorded. This patient's clinical course was virtually diagnostic of gemtuzumab-induced SOS. Although use of defibrotide has been reported to improve 1/3 of patients having SOS in the BMT setting, experience among patients with SOS after gemtuzumab therapy is very limited.

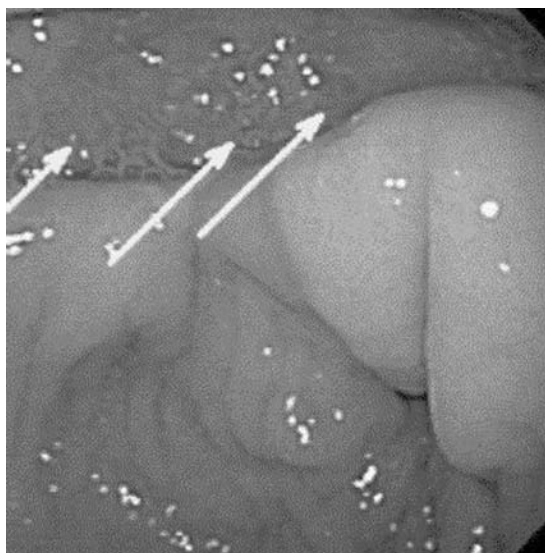
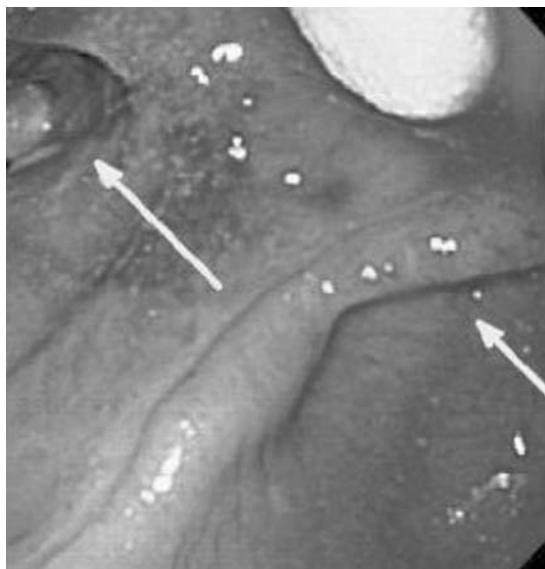
783

**Penetrating Gastric Ulcer: An Unusual Route for Liver Biopsy**

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**Purpose:** There are multiple complications associated with peptic ulcer disease (PUD). Gastric penetration secondary to complicated ulcers have been reported to the pleura, pericardium, and small bowel. We report an unusual case of hepato-gastric penetrating ulcer confirmed by endoscopic imaging and biopsy.

**Case:** A 93 yo female presented with complaints of non bloody vomiting preceded by 2 weeks of dark stools. The patient had recently started coumadin for atrial fibrillation as well as diflunisal for arthritis. Abdominal exam revealed hypoactive bowel sounds, mild epigastric tenderness without rigidity or guarding. X ray did not reveal free air. EGD demonstrated multiple gastric and duodenal ulcers without acute bleeding. 1 large cratered prepyloric ulcer was biopsied and can be seen in Figure 1. This tissue demonstrated normal hepatocytes with mild inflammation. H. pylori stool antigen was negative. Surgical consultation was obtained. Given the pt's age and comorbidities the decision was made to treat her conservatively with strict bowel rest, proton



pump inhibitor, and TPN. Repeat endoscopy in 5 weeks demonstrated complete healing of the gastric ulcer. In Figure 2 the healed gastric mucosa can be seen.

**Discussion:** Asymptomatic PUD is seen most commonly in the elderly. Unlike perforated ulcers, which typically present with a surgical abdomen, penetrating ulcers are more subtle in presentation because they communicate with adjacent organs. However, most penetrating ulcers ultimately require surgery. The most frequently identified organs include duodenum, pancreas, and rarely left lobe of the liver. This patient did remarkably well with aggressive medical management. This is a rare complication of PUD and very unusual route for liver biopsy.[figure1][figure2]

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**De Novo Common Bile Duct Stones Mimicking Malignant Biliary Obstruction**

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**Purpose:** Here, we present an unusual case of a 78 y/o female presenting with significant weight loss, abdominal pain, jaundice and sitophobia. Her Past medical history was significant for osteoarthritis and hypertension. Physical Exam was remarkable for evidence of recent weight loss, mild icterus, a normal liver size and no peripheral lymphadenopathy. Laboratory investigations suggested cholestasis. Imaging studies included a contrast CT of abdomen showing Extrahepatic biliary obstruction and a 9 mm "mass" in the common bile duct with no evidence of any gall bladder stones.

The patient's Primary care Physician had requested tumor markers: CEA, and CA 19-9 Both were moderately elevated. The Patient was referred for an ERCP with a tentative diagnosis of Malignant Biliary Obstruction. However, on ERCP, surprisingly, the patient was found to have a 9 mm isolated common bile duct stone, the cystic duct was patent and no stones could be visualized in the gall bladder. An Endoscopic Sphincterotomy was done and the solitary CBD Stone was extracted. The patient had a sonogram the of the abdomen to definitively exclude gall bladder stones which confirmed absence of any stones in the gall bladder. Patient had a dramatic clinical improvement with resolution of her symptoms, recovery of her weight and normalization of her liver chemistries within a few weeks.

**Results:** Here, we present an unusual case of 78 y/o female with significant weight loss, jaundice, and abdominal pain who on initial investigation of the complaints by a contrast CT of abdomen was reported to have a 9 mm mass in the common bile duct with no evidence of any gall bladder stones. A de novo solitary CBD stone was identified on ERCP and extracted.

**Conclusion:** De novo stones of the common bile duct arise in the setting of 1) recurrent cholangitis 2) congenital anomalies like Caroli's disease 3) sclerosed or strictured ducts 4) very rarely due to mutations in MDR3 gene. Mostly common bile duct stones are a findings associated with cholelithiasis that is a stone arising in the gall bladder passes down the bile duct and becomes symptomatic. Solitary De novo CBD Stones may mimic Malignant biliary obstruction and may falsely elevate tumor markers.

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**Gastric Myeloma**

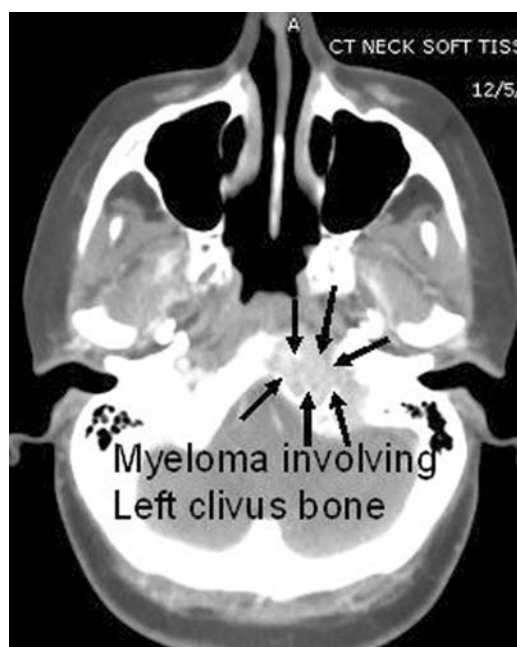
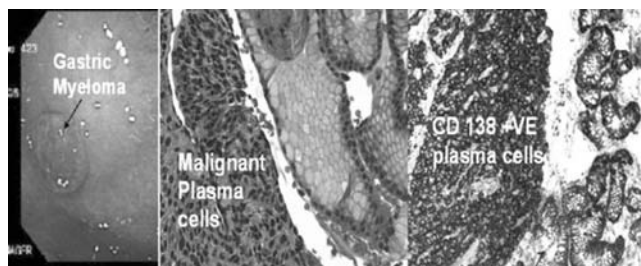
Aman Ali, MD, Louis Rosainz, MD, Eric Rosen, MD, Knarik Arkun, MD, Peter J. Baiocco, MD\*. Gastroenterology and Hepatology, Lenox Hill Hospital, New York, NY.

**Purpose:** A 46 year old female with history of SLE, migraine headaches and CVA presented with nausea, vomiting, progressive solid and liquid dysphagia and headache. Physical examination was unremarkable except for a small, tender, firm mass, palpable in the left submandibular region and left hypoglossal nerve paresis. Pertinent labs revealed macrocytic anemia with normal vitamin B12 and folate levels. LDH was elevated at 810 U/L. A Modified barium swallow revealed oropharyngeal dysfunction. CT scan of

the head and abdomen were normal. Patient continued to vomit for several days and endoscopy was advised.

EGD revealed mild atrophy with linear erosions in the gastric body. A 5 mm, raised, friable lesion was seen in gastric cardia with a "pasted on" appearance (Fig. 1). An excisional cold biopsy was obtained. CT and MRI to evaluate the neck mass revealed an abnormally enhancing, hypervascular mass eroding through the left clivus, jugular foramen and hypoglossal canal (Fig. 2). A stereotactic trans-sphenoidal biopsy of the clivus lesion was planned, however biopsies from gastric lesion reveal atypical mononuclear cells with marked pleomorphism, mitotic activity, multinucleation and positive immunohistochemical staining for CD138 (Fig. 1). These findings are consistent with gastric plasma cell myeloma. Subsequently a bone marrow biopsy revealed sheets of plasma cells. The patient was treated with thalidomide and dexamethasone and transferred to a tertiary center for the remainder of her care.

**Conclusion:** We present an unusual case of multiple myeloma with gastrointestinal manifestations. Although the nausea and vomiting in our patient was most likely from a CNS lesion, endoscopy helped in making a prompt, less invasive, histological diagnosis and contributed significantly to the patient's care.[figure1][figure2]



**Purpose:** This is a case of a 71 year old female who presented to her primary care physician after experiencing dark urine and clay colored stool for one week. She had no other symptoms. Past medical history includes only hypertension and hypercholesterolemia. Physical exam was unremarkable except for slight scleral icterus. Initial laboratory data revealed a total bilirubin of 5.3, AST 166, ALT 278, Alkaline Phosphatase 311, amylase 163, lipase 275 and CA 19-9 267. She underwent abdominal ultrasound which showed dilated intra and extra hepatic ducts, and a hypoechoic structure in the pancreatic head with blood flow. Follow up CT showed a 1.3 cm hypervascular mass in the common bile duct near the head of the pancreas, and extensively dilated intra and extra hepatic ducts. She then underwent outpatient ERCP. A friable mass was protruding from the ampulla, with a filling defect in the mid to distal common duct. The tumor began to bleed with instrumentation, and sphincterotomy with stent placement was performed. A small mucosal tear was clipped. The patient was admitted for observation and serial hematocrits. On hospital day 3 the patient's hematocrit had drifted down to 25 from 42, and she was transfused and underwent repeat ERCP. The tumor was noted to still be oozing. The following day, the patient underwent pylorus preserving Whipple procedure. The patient had an uneventful postoperative course and was discharged on postoperative day 10. Pathology revealed a 4.4 cm periampullary carcinoid tumor with extension into the pancreas and no nodal disease. Carcinoid tumors of the peirampullary region are rare. Current treatment of choice is resection. Patients who undergo Whipple procedure for carcinoid tend to have fewer complications than those with adenocarcinoma. There may be some role for local excision with smaller tumors < 2 cm.[figure1][figure2]



#### Image Label



#### Periampullary Carcinoid Causing Biliary Obstruction

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### A Rare Cause of Nausea, Vomiting and Diarrhea: Eosinophilic Gastroenteritis

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**Purpose:** Eosinophilic gastroenteritis (EG) is rare disease of unknown etiology defined by the presence of gastrointestinal symptoms, eosinophilic infiltration of the gastrointestinal tract, peripheral eosinophilia, and eosinophilic ascites without evidence of parasitic or extra-intestinal disease. EG is classified into mucosal, muscularis, and serosal types. Clinical symptoms include nausea, vomiting, abdominal pain, diarrhea, intestinal obstruction and ascites. Corticosteroids are the treatment of choice.

A previously healthy 27-year old AA female was referred to GI with a two week history of abdominal pain, nausea, vomiting and diarrhea. She did not endorse constitutional symptoms, was on no medications and had not recently traveled. Her physical examination was unremarkable.

Laboratory evaluation: WBC 13,000 (34% eosinophils); stool cultures, O&P, c diff toxin A and B, Entamoeba and Strongyloides were all negative. EGD and colonoscopy were unremarkable. Biopsies of squamous-lined esophagus were notable for 17–20 eosinophils/hpf. Eosinophils were also notable in lamina propria of the duodenum (90/hpf) and colon (75/hpf). One week after endoscopy the patient was seen in a local ED. Abdominal CT scan demonstrated diffuse thickening of small intestinal wall and moderate ascites. Diagnostic paracentesis was significant for 4,128 WBCs with 93% eosinophils. Culture and cytology were negative and evaluation by GYN was unremarkable. Serum IgE levels were elevated.

The patient was placed on oral corticosteroids and at the time of writing this abstract, was responding well.

EG is rare disease that can present in different ways depending on the predominant location of eosinophils. Our patient had transmural involvement based on clinical presentation, endoscopic biopsies and eosinophilic ascites. Although the most common sites of involvement are the stomach and duodenum, our patient had evidence of eosinophilic infiltration throughout the entire gastrointestinal tract from proximal esophagus to distal colon. Talley et al (1990) proposed three main diagnostic criteria for EG: presence of GI symptoms, biopsies showing eosinophilic infiltration in one or more layers and the absence of parasitic infection. Corticosteroids continue to be the preferred treatment. This case demonstrates a rare diagnosis and need for continuous re-evaluation as EG was not in our original differential.

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### Type I Acute Autoimmune Hepatitis in a Male Patient

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**Purpose:** Introduction: Autoimmune hepatitis (AIH) is an unresolving inflammation of the liver of unknown cause. Women develop AIH more often than men (3.6:1). AIH is characterized by interface hepatitis, hypergammaglobulinemia, and autoantibodies. The serologic tests utilized for diagnosis are antinuclear antibodies (ANA), smooth muscle antibodies (SMA) and antibodies to liver-kidney microsome type 1 (anti LKM-1). We present a rare case of acute AIH in a male patient with elevated SMA titers only.

**Case Report:** A 57-year-old male patient was referred for evaluation of abnormal liver function tests. Liver function tests revealed AST of 752 U/L, ALT of 999 U/L and Alk Phos of 117 U/L. He denied jaundice, abdominal pain, abdominal distension, fatigue, malaise or fevers. He had a history of diabetes mellitus, Raynaud's disease, mitral valve prolapse and deep venous thrombosis. His liver enzymes measured nine months ago were within normal limits. He had no recent travel. There was no significant alcohol consumption. Medications included warfarin and exenatide. Physical examination was unremarkable. Iron studies, serum ceruloplasmin and markers for viral hepatitis were negative. ANA, P-ANCA and Anti LKM-1 antibodies

were within normal limits. Patient had elevated SMA titers (1:320) and hypergammaglobulinemia (3.06 gm/dL). CT scan showed mild splenomegaly and porta hepatic lymphadenopathy. Liver biopsy showed active interface hepatitis consistent with AIH. He was started on prednisone and azathioprine. Liver enzymes improved remarkably within two months.

**Summary:** AIH is considered a disease of middle age women. ANA and/or SMA characterize Type I AIH. The present case of a male presenting with SMA as the sole markers of Type I autoimmune hepatitis is considered rare – 3.74% (4/107). SMA and ANA commonly disappear and reappear. Greater importance should be given to laboratory and biopsy evaluation in selected cases.

**Conclusion:** Acute AIH should be considered in the evaluation and work up of men with acute hepatitis of unknown origin even though ANA is negative.

### REFERENCE

1. Czaja AJ. Behavior and significance of autoantibodies in type 1 autoimmune hepatitis. *Journal of Hepatology*. 1999 Mar; 30(3): 394–401.

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### Choledochoduodenal Fistula (CDF) in a Patient Presenting with Seizure

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**Purpose:** A 59 year-old Haitian man presented to our hospital with chronic intermittent vomiting for nearly 10 years. On admission, the patient developed an episode of grandmal seizures for the first time. The patient had a history of hypertension, hypercholesterolemia, chronic renal insufficiency and no prior surgeries. He was on antihypertensive medications and a lipid lowering agent. The laboratory studies revealed: Hgb 12.0 g/l, HCT 36.0%, WBC 9.1 K/mm<sup>3</sup> and PLT 306 K/mm<sup>3</sup>. His serum electrolytes: Sodium 140 mEq/l, potassium 3.1 mmol/l, chloride 68 mmol/l, bicarbonate 58 mmol/l, calcium 9.9 mg/dl, blood urea nitrogen 55 mg/dl, serum creatinine 4.6 mg/dl. The liver profile was normal. The blood PH was 7.41, and urine PH was 9.0. Abdominal sonogram – was intended to evaluate his kidneys – discovered the presence of Pneumobilia. Abdominal CT scan confirmed this finding, and displayed gastric wall thickening with distended duodenum. EGD grossly showed deformed duodenal bulb with an abnormal aperture of 3–4 mm in diameter in the posterior part of the bulb of duodenum. Upper GI series





subsequently showed reflux of contrast material in the non-dilated biliary tree, confirming the presence of CDF (Fig). Later, gastric biopsies indicated positive invasion of helicobacter pylori. During the following days of hospitalization: the renal function improved, the alkalosis resolved, and he was discharged on anti-helicobacter pylori treatment (ampicillin, lansoprazole and clarithromycin). Unfortunately, the patient failed to appear for his follow up appointments.

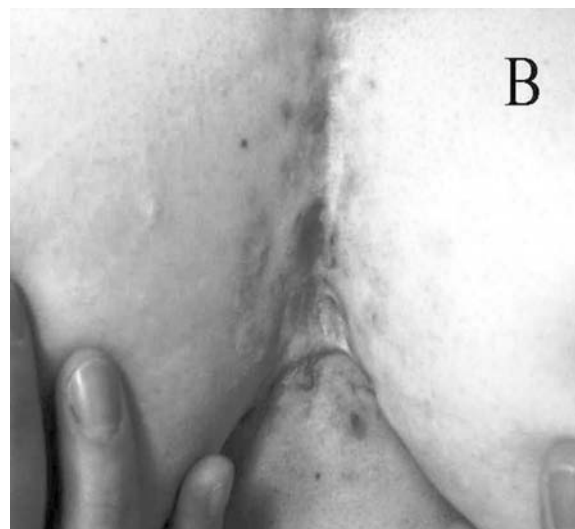
**Conclusion:** Bilioenteric fistulas are usually incidental findings because they seldom produce clinical symptoms. While Cholecystoduodenal fistulas account for ninety percent of bilioenteric fistulas, choledochoduodenal fistulas are rare. Based on our literature search and findings, this is the **first case of CDF** presenting with grand-mal **seizure**. The severe *metabolic alkalosis*, induced by *vomiting* in the setting of *biliary fistula*, appeared to be the contributing disorder. Therefore, physicians should be aware of atypical presentations of CDF and prevent a potentially serious complication.[figure1]

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#### Adalimumab (ADA) Treatment of Hidradenitis Suppurativa (HS) in a Crohn's Disease (CD) Patient

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**Purpose:** HS is a chronic inflammatory disease often causing cutaneous fistulas and scarring. Several reports have associated it with CD. Current therapy for refractory HS is limited and may involve multiple surgeries; however, off-label use of anti-TNF agents has shown some promise. We present a 36-year-old female with a history of CD diagnosed in 1995, started on sulfasalazine and azathioprine who developed HS five years later on her groin, central chest, and under her breasts. Over the next year, she had multiple courses of antibiotics, PO and topical, with little success. She was given three infusions of infliximab (INF) with good resolution in 2001. Her sulfasalazine and azathioprine were stopped during her pregnancy in 2006, and her HS relapsed with painful, malodorous, draining fistulas. She was started on antibiotics, creams, and spironolactone with only minor improvement. INF was restarted; however, she had an infusion reaction with her second dose. The decision was made to start her on ADA, a human monoclonal antibody directed against TNF- $\alpha$ , at 40 mg SC q2W. Over the next five months, her course fluctuated requiring her to receive occasional courses of steroids and one course of antibiotics for possible secondary infection. Meanwhile, she had a surveillance colonoscopy revealing no active disease on biopsy. Her lesions have since ceased draining and causing her pain, however they have unfortunately left her with scars. This report shows that the prior success of treating HS in CD patients with INF can likely be seen with ADA, however further studies are needed to assess the role anti-TNF agents have in the treatment of cutaneous manifestations of CD. According to our literature

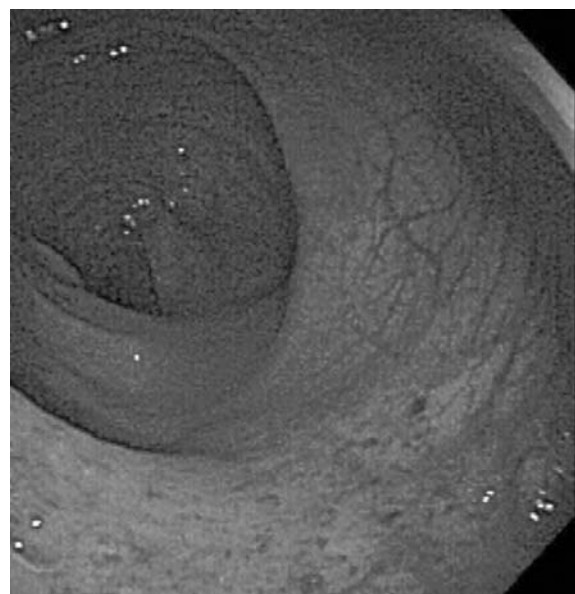


search of the database, this is the first case of successful treatment of HS in a CD patient with ADA, and only one of a few successful reports of HS treated with ADA.[figure1][figure2]

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#### Chronic Intestinal Schistosomiasis

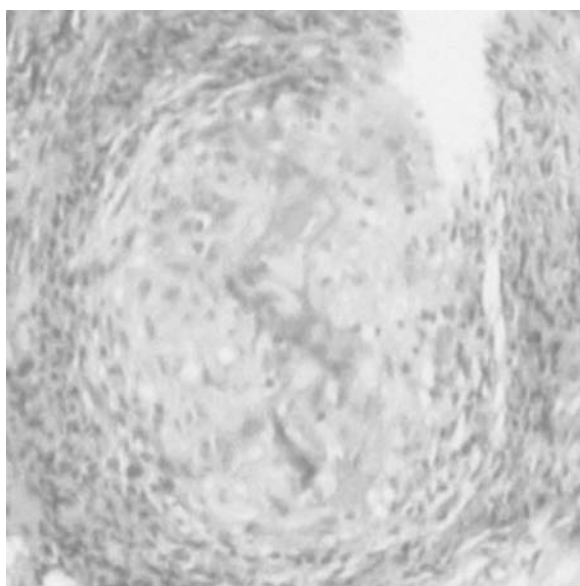
Rishi Pawa, MD, Vishal Gupta, MD, PhD, Rohan Clarke, MD, Jay Cowan, MD, Lisa Ozick, MD\*. Department of Gastroenterology, Columbia University College of Physicians and Surgeons, Harlem Hospital Center, New York, NY.



**Purpose:** Schistosomiasis is a common parasitic disease in the tropical and subtropical regions of Asia, Africa and South America. The disease is caused by a parasitic blood fluke that resides in fresh water. We report a case of a 24 year old male from Ghana without previous bowel problems, who presented with a history of diarrhea of six months duration. The diarrhea was



non-bloody and watery in nature with an estimated frequency of four to six episodes per day, associated with rectal tenesmus, abdominal discomfort and a five lbs weight loss. There was no history of fever, arthralgias, skin lesions or visual symptoms. Physical examination was remarkable for mild abdominal tenderness located primarily in the hypogastrium with no rebound. Laboratory studies including a complete blood cell count, chemistries and stool studies for ova and parasites were unrevealing. Colonoscopy performed subsequently showed erythematous mucosa of the distal sigmoid colon and the rectum. [figure1] Histological examination of rectosigmoid biopsy showed multiple giant cell granulomas and a single *Schistosoma* egg with a terminal spine. [figure2] Biopsies obtained from the remainder of the colon and terminal ileum were within normal limits. Patient was treated with a single dose of Praziquantel (40 mg/kg) with complete resolution of symptoms. Thus, we conclude that even though schistosomiasis is not endemic in the United States, it should be considered in the differential diagnosis of patients with gastrointestinal symptoms, particularly in travelers and former residents of endemic areas.

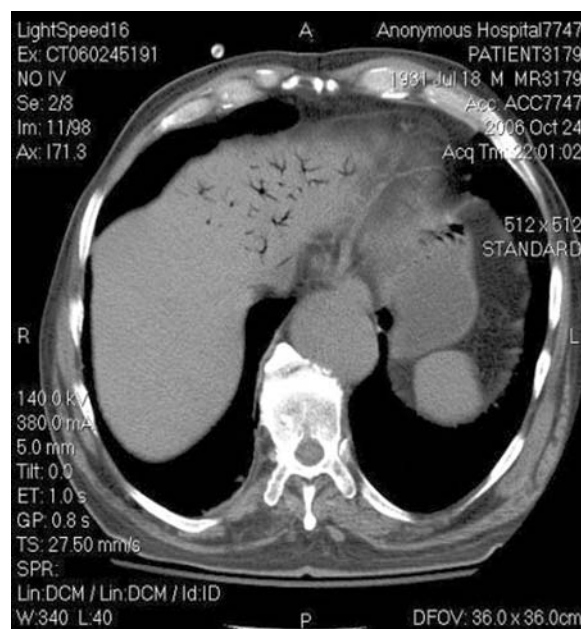
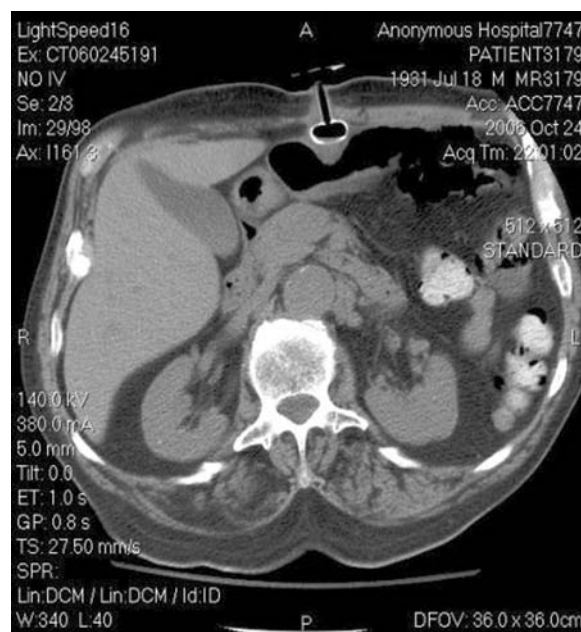


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### The Buried Bumper Syndrome and Gas in the Portal Venous System

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**Purpose:** A case of Buried Bumper Syndrome accompanied by gas in the hepatic portal venous system is reported. A 77 year-old man with a recent stroke and percutaneous gastrostomy (PEG) tube placement two months previously for dysphagia was admitted to our institution with complaints of acute pain at the PEG tube site. An abdominal computed tomography revealed that the internal bumper had migrated from the gastric lumen into the abdominal wall, otherwise known as the Buried Bumper Syndrome. Incidentally, gas was also discovered in the portal venous system. With the advancement of CT imaging, the incidence of detecting hepatic portal venous gas has risen. Traditionally associated with a grim prognosis, hepatic portal venous gas has now been linked to a wider array of pathologies. After undergoing an endoscopy, with removal of the buried internal bumper and replacement of the PEG tube, the patient had an uneventful recuperation. To our knowledge, there have been no cases reported of gas in the portal venous system coinciding with the Buried Bumper Syndrome.[figure1][figure2]



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### Whose Call Is This? Could There Be a Common Explanation for All These Seemingly Unreal Tragedies? Since the Root Cause Is Preventable and Related to Liver, Let Us Try To Elucidate It

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**Purpose:** To increase awareness about MCAD. MCAD is very common metabolic disease (1 in 80). Still not well-known even among physicians. There are many precipitating factors (like fasting, starvation, excessive physical activities, infection, alcohol consumption or surgery) and protean clinical manifestation -vomiting, lethargy, confusion, unexplained tachycardia and fatal ventricular arrhythmia, it is still a mysterious illness. It is very well written about, quite common but still not often entertained in differential diagnosis.

**Methods:** WHAT COULD BE COMMON IN ALL THESE CASES? 29 years old runner dropped dead after Philadelphia half marathon. -Philadelphia Inquirer.

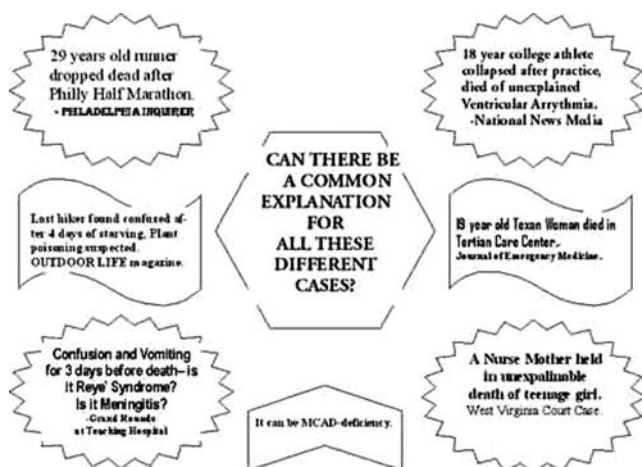
Confusion and vomiting for 3 days before death-is it Reye's syndrome? Is it Meningitis? -Grand Round at Teaching Hospital. 19 years old Texan Woman died in Tertiary Care Center. -Journal of Emergency Medicine A Hiker found confused after being lost for 4 days, Plant poisoning suspected. -Outdoor Life. A Nurse mother held in unexplainable death of teenage girl.-West Virginia Court Case.

An 18 year college athlete collapsed after practice, died of Ventricular Arrhythmia. -National News Media.

**Results:** To avoid these tragedies, we need to understand "METABOLIC END POINT". With physical training, one can improve the cardiopulmonary reserve, but cannot change this MEP. The stressors mentioned above leads to depletion of carbohydrate as energy source and ketotic pathway of metabolism kicks in. During this the long chained stored fat molecules are broken into acetoacetate and b-hydroxybutyrate. While in a person with MCAD deficiency, the break down of long chained fat is halted to 6 to 10 carbon chain particles. This increased production of medium chained fat particles accumulates in various body organ causing variety of clinical presentation mentioned above.

**Conclusion:** The best way to avoid this kind of tragedy is to create public awareness and avoid the events that lead to MEP.

To avoid the tragedy in the people who want to push their limit of physical activities, Maintain proper hydration, supply of glycogen for energy and avoid ketogenic diet, are other important factors.[figure1]



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### Proton Pump Inhibitors Masking a Zollinger Ellison Syndrome

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**Purpose:** Zollinger Ellison syndrome is a well described clinical entity manifested by hypersecretion of gastric acid, proximal small bowel ulceration, and non-beta islet cell tumors of the pancreas with aggressive metastatic potential. Initial symptoms are often vague and can mimic benign ulcer disease or functional abdominal pain. Response to empiric antisecretory therapy often results in delayed workup with potential serious implications. We present a case of 42-year-old female with classic symptoms of ZE syndrome including dyspepsia, GERD, and diarrhea that drastically improved on high dose PPI therapy. Because she responded well to empiric therapy, no further workup was pursued. She presents four years later with painless jaundice and recurrence of symptoms after PPI therapy is halted. Further evaluation

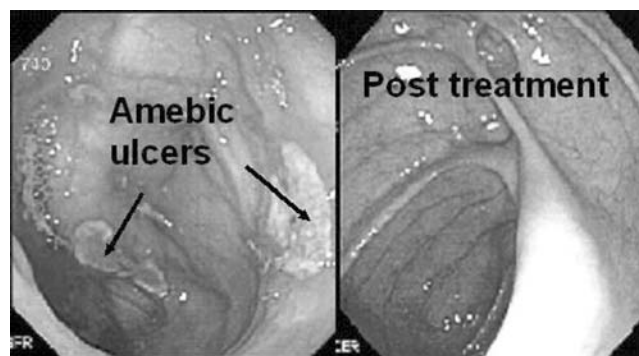
with abdominal imaging reveals a 6 cm calcified pancreatic head mass obstructing her biliary tree with a single liver lesion suspicious for metastatic disease. Therapeutic ERCP reveals multiple small bowel erosions raising the suspicion of a ZE syndrome. Baseline serum gastrin levels are 3852 pg/ml off PPI, with normal IgG4 levels. Octreotide scan reveals intense activity in the pancreatic head and in a focal area of the liver worrisome for metastatic disease. Whipple procedure with wedge resection of the liver lesion confirms the diagnosis of a metastatic gastrinoma. This case demonstrates the pitfalls that can occur with empiric treatment of dyspepsia without complete evaluation especially when diarrhea is one the chief complaints. Although Zollinger Ellison syndrome accounts for less than 1% of peptic ulcer disease in the United States, early diagnosis is crucial to avoid development of peptic ulcer disease complications and metastatic disease.

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### Amebiasis Mimicking Metastatic Colon Cancer

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**Purpose:** A 66 year old male with no past medical history presented with 2 days of crampy, non-radiating, right lower quadrant pain. The patient denied fever, change in bowel pattern, abdominal distention, nausea, vomiting or rectal bleeding. The patient had traveled to West Africa three months ago where he admitted to drinking well water and having a self-limited diarrheal illness. However since his return to United States, he was asymptomatic. On physical examination, he was afebrile, abdomen was soft and non-distended but right lower quadrant was tender on deep palpation. There were no peritoneal signs, palpable masses or viscera. Rectal exam was normal.



CBC revealed WBC count of 18.1 without eosinophilia. A CT scan of abdomen and pelvis displayed wall thickening in the cecum and ascending colon, minimal stranding of the pericecal fat and a few low attenuation lesions in the liver (Fig. 1). These findings were worrisome for colon neoplasm with metastasis to the liver. He underwent colonoscopy that revealed numerous non-bleeding serpiginous ulcerations in the cecum and right colon (Fig. 2). The ulcers were well circumscribed with raised margins and central necrotic base and in conjunction with his travel history, were suspicious for amebic infection. Biopsies did not show amebic organisms but displayed marked

chronic active inflammation, increased eosinophils, paneth cell metaplasia, crypt distortion, and fibrinopurulent exudates and were considered consistent with amebic infection. Amebic antibody titers were abnormally high. Patient was treated with metronidazole and paromomycin for 10 days with a remarkable clinical recovery. Colonoscopy and CT scan performed two months later confirmed resolution of the infectious process (Figs. 1 & 2). [figure1][figure2]

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### Methotrexate in Autoimmune Hepatitis

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**Purpose:** Methotrexate has been used in patients with cholestatic liver disease and granulomatous hepatitis, however there has been only three published reports on its use in Autoimmune hepatitis (AIH). Standard treatment regimens for AIH includes corticosteroids and purine analog azathioprine. Treatment options for patients refractory or intolerant to standard therapy are limited. This includes medications as Mycophenolate Mofetil, Tacrolimus, Cyclosporine and Methotrexate. **METHODS:** We describe a 44-year-old Hispanic female with no history of alcohol abuse who presented with jaundice, ascites, elevated liver enzymes AST: 525, ALT: 275, positive ANA: >1:5120 and SMAB >1: 80. Viral hepatitis serology and rest of chronic hepatitis work-up was negative. Liver biopsy was consistent with autoimmune hepatitis and cirrhosis. Liver enzymes did not normalize with prednisone alone. Patient was started on azathioprine but developed pancreatitis. Mycophenolate Mofetil was also tried but patient developed intolerable side effects and was discontinued. Methotrexate at 7.5 mg po per week resulted in normalization of liver enzymes and maintenance of remission with a steroid sparing effect. Patient refused repeat liver biopsy. To date, 18 months after starting methotrexate, patient is asymptomatic with normal liver function tests, resolution of ascites and off steroids. **CONCLUSION:** In this case methotrexate was used successfully with normalization of liver function tests and steroid sparing effect with no documented side effects. These findings suggest that methotrexate may be useful in treatment of autoimmune hepatitis intolerant or refractory to standard therapy.

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### Recurrent Lymphoma Presenting as Incarcerated Umbilical Hernia

Eyong J. Ly, BA, Edward R. Feller, MD\*, Fred J. Schiffman, MD. Department of Medicine, Warren Alpert Medical School of Brown University, Providence, RI.

**Purpose:** Tumor-associated incarcerated umbilical hernia is rare. Similarly, this severe complication is an exceptional initial manifestation of recurrent malignancy. We report a patient with acute incarcerated hernia as the presenting feature of relapsed lymphoma.

**Case report:** A 62-year-old woman with a history of large-cell lymphoma in remission for 2 years presented with increasing epigastric pain and mild nausea for 5 days. She had a known, asymptomatic umbilical hernia for many years. On exam, she was afebrile, tachycardic, and normotensive. Abdominal exam revealed a soft, mildly distended abdomen with an incarcerated hernia that was erythematous and exquisitely tender to palpation. Ascites was not present. Laboratory studies showed Hgb = 12 Gm%; WBC = 14,400 with 78% Neutrophils, 1% Bands, and 15% Lymphocytes. Abdominal upright and lateral decubitus x-rays revealed no air-fluid levels. At urgent laparotomy, she had an incarcerated hernia containing edematous, inflamed, viable omentum without bowel. Histology of the hernia sac showed a clonal lymphoid population present within the sac that was consistent with recurrent diffuse, large B-cell lymphoma. The patient did well post-operatively and was discharged home one week after admission.

**Discussion:** Malignancy may involve the umbilicus by contiguity, lymphatic or venous spread or by arterial emboli. Palpable, non-tender skin or sub-

cutaneous metastasis, termed Sister Mary Joseph's nodule, may rarely occur. Pain and tenderness may also be sub-acute, or slowly progressive. Tumors in incarcerated hernias are rare, reported in intra-abdominal or pelvic carcinoma as well as by uterine fibroids, umbilical varix, endometriosis, and pseudomyxoma peritonei. Increased pressure due to pregnancy, ascites or tumor may potentiate incarceration. Skin ulceration, necrosis, strangulation or hernia rupture may occur. Incarcerated hernia is an exceptional presenting feature of an undiagnosed or recurrent tumor. As illustrated in this case, clinicians should consider underlying malignancy when a chronic, asymptomatic umbilical hernia suddenly incarcerates.

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### Safe Use of the PillCam ESO in a Patient with an Implantable Cardioverter Defibrillator

Daniel S. Mishkin, MD, CM\*. Gastroenterology, Boston University, Boston, MA.

**Purpose:** There has been concern regarding the use of capsule endoscopy in patients who have an electromedical device based on the fact that both agents work on a similar radiofrequency. While it is a contraindication to use the PillCam in a patient with an implantable electromedical device, many are performing the test on a case-by-case scenario. This is the first published report using PillCam ESO in such a patient.

A 62 year old man presents for evaluation of his progressive liver disease that is secondary to Hepatitis B and excessive alcohol use. He serologically has evidence of cirrhosis and no history of gastrointestinal bleeding. His past medical history is significant for a dilated cardiomyopathy with an ejection fraction of 15% for which he takes coumadin and he had an automatic implantable cardioverter defibrillator (Guidant Contak Renewal 3-CRT-D) implanted. An evaluation of his esophagus was recommended regarding the potential for primary prophylaxis, should he have varices. After a discussion with the patient about the different options of evaluation, he chose to swallow the PillCam ESO. In light of his cardiac status, risk of bleeding, inability to get a ride home, and patient preference, there were multiple reasons why he chose to avoid an esophagogastroduodenoscopy.

During the time of the procedure, the patient was closely monitored. The pulse generator was located in the left upper chest wall, in relative close proximity to the 3 sensors for the study. There were no apparent cardiac changes, both clinically and on the monitor in this pacemaker dependent subject. After completion of the exam marked by the change in the lights on the data recorder signifying no further transmission, he was monitored for an additional 5 minutes.

The images acquired demonstrated an abnormality in the esophagus that on further evaluation was consistent with high grade dysplasia in a short segment Barrett's esophagus and no varices. There was no loss of images acquired during the examination.

Several series have performed capsule endoscopy in such patients without interference to the implantable electromedical device or image acquisition. In one study there was a loss of the images while the capsule was in close proximity to a patient's abdominal pacemaker pulse generator. This was a specific concern as in a study using the PillCam ESO, as the sensor arrays are in the vicinity of the pulse generator. However, in this case, there was no loss or alterations of the images during the 22 minutes of the study.

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### A Simple Twist of Fate?

Ryan M. Ford, MD, Kristina R. Chacko, MD, Tanvi Dhere, MD, Greg Nesmith, MD, Henry Olejeme, MD\*. Division of Digestive Diseases, Emory University School of Medicine, Atlanta, GA.

**Purpose:** A 19 year old Hispanic female who was 28 weeks pregnant was admitted for seizures and recurrent post-prandial nausea, vomiting, and abdominal pain. Her symptoms had been present throughout the entire pregnancy. Her past medical history included a diagnosis of epilepsy at age 11.

She had no known drug allergies. Her medications included anti-epileptics, prenatal vitamins, folic acid, and anti-emetics. Family history was notable for hypertension and diabetes. She did not smoke or drink alcohol. Vital signs were notable for a mildly elevated blood pressure and a mild tachycardia. Physical exam revealed a gravid abdomen with mild epigastric tenderness and mild lower extremity edema. Labs revealed low albumin, electrolyte abnormalities, acute renal failure, mild proteinuria, and elevated liver enzymes. A previous right upper quadrant ultrasound showed sludge in the gallbladder, and a single view chest radiograph showed moderate gastric distension. Out of concern for pre-eclampsia and an atypical HELLP syndrome, the patient underwent an urgent C-section.

Five days post-operatively, the patient developed recurrent nausea and vomiting while receiving narcotics. She was given anti-emetics but she experienced an episode of coffee ground emesis after a nasogastric tube was placed. Vital signs were stable and physical exam was again only notable for mild epigastric tenderness. Repeat bloodwork was unremarkable. Chest and abdominal radiographs were normal. Upper endoscopy revealed a distended stomach containing greater than two liters of retained fluid, as well as a sharp turn in the second portion of the duodenum. A CT scan showed multiple embryological defects in addition to findings consistent with intestinal malrotation. An upper GI series confirmed the diagnosis. The patient went to the operating room for a laparoscopic appendectomy and duodenocolonic dissociation (LADD procedure). She was discharged five days later. Intestinal malrotation requiring surgery usually presents in the first month of life. It is less common to present in adulthood. In this case, we hypothesize that pregnancy, with its associated changes in intra-abdominal anatomy, precipitated the clinical presentation of intestinal malrotation. This case also demonstrates many of the classic findings, work-up, and treatment of this embryological defect. Intestinal malrotation is a rare disorder that may present with common symptoms in adults.

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#### Cholestatic Hepatitis Associated with Hyperthyroidism, and Exacerbated by Methimazole Therapy

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**Purpose:** Cholestasis can be caused by multiple drugs and systemic disorders. It is clinically important that reversible conditions are detected rapidly and corrected. A 28-year-old Pakistani man presented with 1 month history of progressive jaundice. He had a medical history of hyperthyroidism diagnosed recently for which he was treated with methimazole 10 mg PO TID for one month. No history of alcohol use. Clinical chemistry parameters two weeks prior to methimazole therapy were as follow; total bilirubin 5.8 mg/dL, direct bilirubin 3.2 mg/dL, alkaline phosphatase 227 U/L, AST 43 U/L, ALT 51 U/L, Free T4 4.19 ng/dL, and TSH 0.03 uIU/mL. On admission his total bilirubin level was 40.4 mg/dL, direct bilirubin 26.1 mg/dL, alkaline phosphatase 256 U/L, AST 36 U/L, ALT 42 U/L, lipase 32 U/dL, Free T4 3.5 ng/dL, TSH 0.03 uIU/mL. Markers for autoimmune hepatitis and viral hepatitis A, B, and C were negative. A CT scan and ultrasound of abdomen were normal with no biliary dilatation. Liver biopsy showed prominent bile stasis, and minimal portal and occasional parenchymal neutrophilic infiltrate. No fibrosis was found. At the time of admission, methimazole was discontinued and we observed a rapid decrease in the levels of bilirubin, alkaline phosphatase and liver enzymes, however these were still above normal values. The patient was subsequently started on lithium to control his hyperthyroidism. As he remained hyperthyroid he received radioablation of the thyroid gland two months after lithium was started. Six months after this procedure his levels of bilirubin, alkaline phosphatase, and liver enzymes decreased to normal levels. Hyperthyroidism has been associated with cholestatic hepatitis that is usually not clinically evident. The liver injury described with hyperthyroidism is reversible after appropriate treatment of the disease. Methimazole is rarely associated with cholestatic liver injury

that is reversible within months after its discontinuation. In patients with hyperthyroidism and baseline liver enzymes abnormalities, it is important to monitor the liver enzymes after methimazole is started.

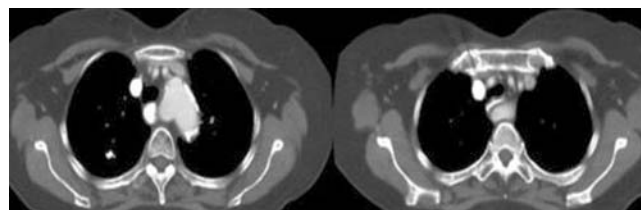
## 801

#### Dysphagia Lusoria Due to an Aberrant Right Subclavian Artery and a Dilated Diverticulum of Kommerell

*Srikanth Vallurupalli, MD, Juan Jimenez, MD\*. Internal Medicine, University of Illinois at Urbana Champaign, Urbana, IL and Radiology, University of Illinois at Urbana Champaign, Urbana, IL.*

**Purpose:** We describe an uncommon vascular cause of dysphagia in the elderly.

**Methods:** A 72 year old woman complained of intermittent dysphagia to solid food. She reported no loss of appetite or weight loss. Physical examination was unremarkable. A barium esophagogram revealed mass effect at the junction of the proximal and middle thirds of the esophagus.[figure1] Computed tomography of the chest was performed and demonstrated the presence of a left sided aortic arch and an aberrant right subclavian artery arising from a diverticulum of Kommerell.[figure2] The dilated diverticulum and the artery displaced and compressed the esophagus and trachea. Surgical correction was not attempted due to the minimal nature of symptoms.



**Results:** Bayford in 1787 described extrinsic compression of the esophagus by aortic vascular abnormalities as a result of “Lusus Naturae” meaning

a freak of nature which eventually lead to the term dysphagia lusoria. An aberrant right subclavian artery occurs in about one percent of the population but is usually asymptomatic. This aberrance is the result of the persistence of the seventh intersegmental artery during the involution of the fourth aortic arch resulting in its retro-esophageal course. Kommerell in 1936 described a diverticulum at the origin of the aberrant artery in a patient with a left sided aortic arch as a remnant of the primitive right dorsal aorta. With the development of atherosclerosis, the aorta and its vessels become rigid and tortuous leading to symptoms in the elderly. Several surgical techniques have been described to relieve the compression but are only performed after careful consideration of the risks and benefits.

**Conclusion:** Clinicians should be aware of this rare cause of dysphagia which as the population ages, may present more often.

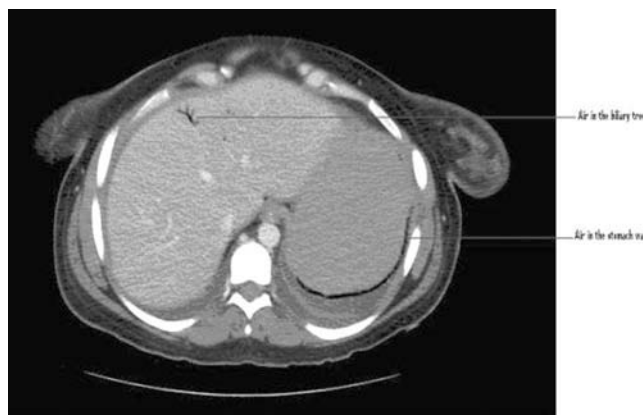
802

### Emphysematous Gastritis Due to Infection from a Non Gas-Producing Bacteria!

Manju P. Paul, MD, Savio John, MD, Nilesh Mehta, MD, Preeti Mehta, MD, Uma K. Murthy, MD\*. Medicine, SUNY Upstate Medical University, Syracuse, NY.

**Purpose:** Emphysematous gastritis is a rare condition in which gas collects within the stomach wall secondary to infection by gas-producing bacteria. We report the case of 25 year old female with neurofibromatosis who developed diffuse abdominal pain and distension after C-section. There was no history of alcohol or substance abuse, ingestion of corrosive substances or NSAIDs. Patient was febrile, tachycardic, and tachypneic and appeared toxic. Abdomen was markedly distended and tender with absent bowel sounds. Blood work showed WBC count of 25,000 with 91% neutrophils. CT of the abdomen showed gastric pneumatosis along the entire greater curvature and biliary tree, diffuse dilatation of the stomach, small bowel and large bowel. EGD showed diffuse severe mucosal abnormality with congestion, discoloration, granularity, texture change, decreased vascular pattern and ulceration on the posterior wall and greater curvature of the stomach. Gastric biopsy revealed transmural necrosis and streptococcus viridans and stomatococcus were isolated. Patient was started on clindamycin and piperacillin/tazobactam as well as IV hydration and TPN from the first day. Patient improved with the above measures and was discharged home after 10 days of hospital stay. Follow up CT scan and EGD showed resolution of the previous findings. It is important to differentiate emphysematous gastritis from gastric emphysema as

early institution of antibiotic therapy covering anaerobes and gram negative bacilli, along with IV hydration and institution of nutrition is the mainstay of treatment. The stomach is a very uncommon site of involvement, due to abundant blood supply, acidity and efficient mucosal barrier. Currently, CT is the best imaging study for diagnosis of emphysematous gastritis. Surgery is avoided during the acute phase of infection due to friability of the gastric mucosa.[figure1][figure2]



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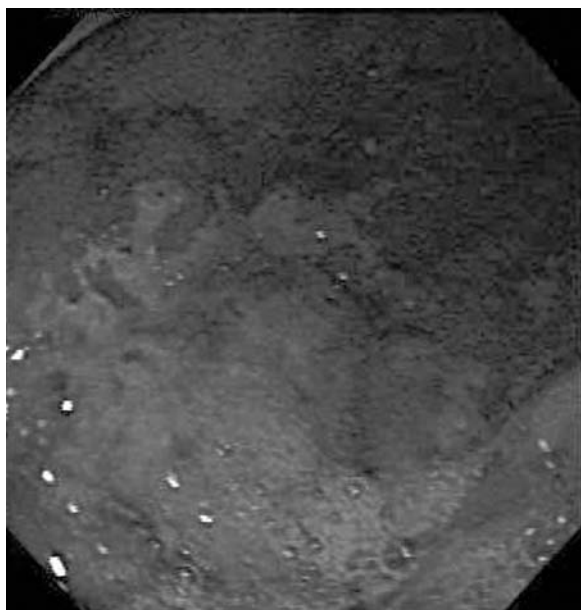
### Identification of Unsuspected Parasitic Disease on Video Capsule Endoscopy

Nirmala M. Sivaprakasapillai, MD, Thomas Judge, MD\*. Gastroenterology, Cooper University Hospital, Camden, NJ.



**Purpose:** Parasitic infection has been rarely identified utilizing video capsule endoscopy (VCE). We report the case of a 41 year old Puerto Rican male who underwent VCE for evaluation of hematochezia and was found to have parasitic infection.

**Methods:** Complete blood count was in the normal range. The patient underwent VCE after an unrevealing upper endoscopy and colonoscopy. At the time of the VCE, the patient was noted with 2 parasites in the colon. [figure1] They were colorless and estimated to measure approximately 2–3 mm. He



was asymptomatic and three stool samples failed to isolate the organism. There was no peripheral eosinophilia.

**Results:** Based on the appearance of the parasite and history of travel to Puerto Rico, *Strongyloides* infection was suspected. *Strongyloides* antibody titer by ELISA was 1.58 which was in the equivocal range (titer of 2.11 or greater is a positive test). The patient was treated with two doses of Ivermectin, given two weeks apart and repeat antibody titer by ELISA had decreased to 0.68 (titer of 1.49 or less is a negative test).

**Conclusion:** Review of the literature revealed rare reports of parasite identification by VCE. When identified, it is typically an incidental finding that is beneficial in treatment of an otherwise asymptomatic patient.

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#### Intermittent Jejunostomy Tube Obstruction Due to *Ascaris Lumbricoides* Infection

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**Purpose:** Ascariasis is the third most frequent helminthic infection in the US. The female worm can measure up to 40 cm in length. We describe a patient who presented with J-tube occlusion from *A. lumbricoides* infection.

**Case:** A 45-year-old Costa-Rican woman was referred due to jejunostomy tube malfunction. Initially, she was admitted after sustaining a closed head injury in a MVA near the Arizona-Mexico border. She remained nonverbal and required assisted ventilation and a J-tube placement for nutrition. Since her tube placement, multiple episodes were noted where nutritional formula could not be administered through the tube. No residual tube feeds were noted. There was no visible kink or damage and no clinical or radiological evidence of small bowel ileus/obstruction. She was afebrile with stable vital signs and abdomen was benign with normo-active bowel sounds. Her jejunostomy site appeared clean and intact. The WBC count was 6,400 with 5% eosinophils, hemoglobin 10.6, MCV 85 and platelet 351,000. Her LFTs were normal.

A gastrograffin injection of the J-tube revealed no evidence of leak and the tube was in appropriate position. An EGD revealed a mobile roundworm in D2 extending distally.[figure1] Upon endoscopic removal this measured 5 inches in length. Pathology confirmed this to be *A. lumbricoides*. She was treated with mebendazole 100 mg BID  $\times$  3 days and subsequently had no further episodes of tube obstruction.



figure 1

**Discussion:** More than 1.4 billion people are infected with *Ascaris* worldwide with the highest prevalence in tropical countries. Transmission occurs mainly via ingestion of water/food contaminated with eggs. Adult worms inhabit the lumen of the small intestine, but may be found anywhere in the GI tract. Common GI manifestations of infection include abdominal pain; intestinal, hepatobiliary and pancreatic duct obstruction.

Intermittent occlusion of this patient's jejunostomy tube was likely the result of obstruction from ascariasis infection, which was treated both medically and endoscopically. Although infections in adults are rare in the US, unusual manifestations of parasitic infections should be considered in those from endemic areas.

805

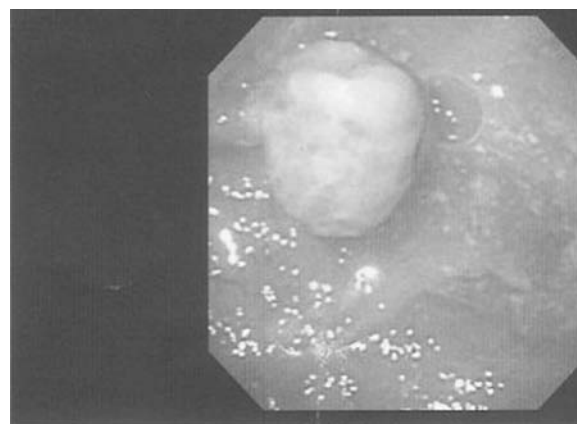
#### Colonic Polyps in the "Esophagus"

Jessica Widmer, DO, Paul Panzarella, MD, William Gusten, MD, Kavita Kongara, MD\*, James Grendell, MD. Gastroenterology, Winthrop University Hospital, Mineola, NY.

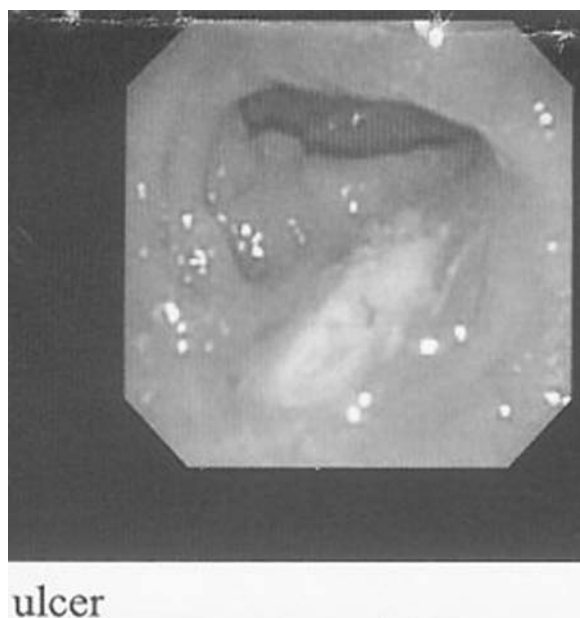
**Purpose:** Esophageal atresia is a condition in which the proximal and distal portions of the esophagus do not communicate. Etiologies of these anomalies are still largely unknown; however, vascular insufficiency, genetic factors, vitamin deficiencies, drug and alcohol exposure, viral, chemical, and physical events have all been linked to embryologic developmental aberrancy.

Our patient is a 32 y.o. male with esophageal and duodenal atresia corrected by gastrojejunal anastomosis and colonic interposition as an infant. He presented with nausea, melena, hematemesis, and a syncopal episode. His medical history was remarkable for dysphagia and recurrent pneumonias. On admission, UGI and SBS revealed colonic interposition with segments of the jejunum anastomosed to the stomach, proximal duodenum, and biliary system. Gastric varices, an ulcer in the fundus, and inflammatory changes in the duodenal bulb were suspected. Upper endoscopy however, revealed a non-bleeding 1.5 cm neo-esophageal /gastric ulcer at the anastomosis site, and a 1 cm sessile polyp in the proximal neo-esophageal transposed colon. This was removed via snare cautery polypectomy and was later histologically confirmed as a juvenile retention polyp.

Multiple studies of patients with interposition report post-operative complications such as motility problems, gastroesophageal reflux, and respiratory complications.<sup>1</sup> The endoscopic findings and history of recurrent pneumonia in our patient confirm these findings. Cases of adenomatous polyps and adenocarcinoma in transposed colonic segments to correct esophageal atresia have also been reported. This illustrates the need and re-emphasizes the importance of colon cancer screening wherever colonic tissue is found. 1. Deurloo et al, "Esophageal function after correction of esophageal atresia: follow-up after more than 18 years." *Eur J Gastroenterol Hepatol.* 2005; 17(1): A27.[figure1][figure2]



polyp in neo-esophagus



806

#### Oro-Nasal Fistula: An Usual Etiology of Dysphagia after Treatment for Tonsillar Cancer

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**Purpose:** Surgery and chemo-XRT are commonly used to treat tonsillar cancer.

Post-XRT dysphagia is common, and results acutely from mucositis and xerostomia. Late complications include trismus, dental decay, osteoradionecrosis, proximal esophageal strictures and cranial nerve dysfunction. We present an unusual patient who presented with dysphagia and nasal regurgitation secondary to an oro-nasal fistula following chemo-XRT for recurrent tonsillar cancer, diagnosed by endoscopy.

**Case report:** This 59 y/o Hispanic male with a history of T1N0 SCCa, of the left tonsil was treated initially with wide local resection. Chemo-XRT was administered for recurrent cancer at 1 year. He presented with gradually progressive solid food dysphagia and left nasal regurgitation.

A complete physical examination was unremarkable. ENT evaluation including a flexible endoscopy was negative for recurrent cancer. An MRI of the neck (Fig. 1) found no evidence of enhancement in the upper neck, skull base, or within the cranium.

DVE showed slightly diminished swallowing function but was otherwise unremarkable. An upright barium swallow (Fig. 2) was completed and initially reported to be normal. An EGD was performed to exclude a metachronous esophageal cancer and other stenoses. EGD showed normal esophagus, stomach and duodenum. In the oropharynx, on the left and lateral of the uvula an opening was visualized (Fig. 3). The scope was easily passed through this opening to the nasopharynx where the turbinates were clearly visualized, confirming the finding of an oro-nasal fistula. Although the diagnosis was elusive, management was relatively simple and included prescription of a palatal obturator to be placed to occlude the fistula.

Oro-nasal fistula is an inadequately recognized consequence of surgery and XRT for tonsillar Ca. Awareness and timely recognition of this entity is crucial in managing these patients as a simple prosthetic device makes a tremendous difference to the patient's suffering and allows meeting nutritional goals.

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#### Case Report: Argon Plasma Coagulation for the Treatment of Hemorrhagic Radiation Sigmoiditis

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Gastroenterology, University of Alberta, Edmonton, AB, Canada.

**Purpose:** Radiation colitis is not an uncommon consequence of pelvic radiation, such as in patients treated for gynecologic cancers. Some of these patients may suffer from anemia requiring transfusion due to chronic bleeding. Many of these patients are managed with rectal medications, which is often inadequate for control. Argon plasma coagulation (APC) has been well described for its efficacy in treating radiation proctitis. Here, we present two cases in which APC therapy was used to treat radiation sigmoiditis.

**Methods:** We followed two cases originally seen at our regional cancer centre (Cross Cancer Institute) in Edmonton, Alberta, Canada. Both patients received pelvic radiation for endometrial cancers and were referred for active bleeding secondary to radiation colitis that had required numerous transfusions.

**Results:** Radiation induced telangiectasias were found from 10–50 cm in the sigmoid colon. Both patients had significant improvement of symptoms after one session of APC treatment set at 40–60 W and gas flow of 2.0 L/min. To assess the efficacy of treatment, a second endoscopy with APC was performed. There were no complications from the procedures. Neither patient require blood transfusions after the initial treatment with improvement in their hemoglobin levels and were doing well at four and ten-month follow up.

**Conclusion:** Argon plasma coagulation can be used effectively to provide immediate and sustained resolution of symptoms in patients with radiation sigmoiditis (colitis).

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#### Intestinal Occlusion Caused by Meckel's Diverticulum with Ileocecal Intussusception in an Elderly Patient: A Rare Case Report

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**Purpose:** We present a successfully treated case of small bowel obstruction secondary to Meckel's diverticulum with ileocecal intussusception. A 75 year old male with chronic constipation presented with confusion, vomiting and diarrhea. On admission he had hypotension, tachycardia and tachypnea. There were some rhonchi and few crackles in both lungs. His abdomen was diffusely distended, non-tender with normal bowel sounds. Investigations revealed WBC of 6300/mm<sup>3</sup> (78% neutrophils), CK: 605 U/L (N: 22–269 U/L), arterial blood gas showed hypoxemia, blood urea nitrogen of 77 mg/dl (N: 7–18 mg/dl) and Creatinine of 3.9 mg/dl (0.5–1.2 mg/dl). Hepatic panel and serum electrolytes were normal. Chest radiograph showed bilateral infiltrates and abdominal CT revealed high grade distal partial small bowel obstruction. He was started on Piperacillin/tazobactam and Zithromax for sepsis secondary to aspiration pneumonia, fluid resuscitation and nasogastric suction for partial small bowel obstruction. His blood cultures and urine culture were negative. C. difficile toxin, mycoplasma and legionella were negative. Repeated abdominal CT showed high grade small bowel obstruction proximal to the middle ileum with moderate wall thickening. Laprotomy showed small bowel obstruction secondary to Meckel's diverticulum with ileocecal intussusception. A small bowel resection was performed and the patient recovered very well.

**Discussion:** Meckel's diverticulum, the most common congenital anomaly of the gastrointestinal tract, occurs in 1–3% of the population. Majority of patients with Meckel's diverticulum are asymptomatic and only less than 5% of these patients have clinical presentations, such as intestinal obstruction, intussusceptions, inflammation and bleeding. Further, symptomatic Meckel's diverticulum is primarily found in pediatric age and virtually nonexistent in elderly. It is difficult to diagnose Meckel's diverticulum before operation. Meckel's diverticulum should be searched in the laparotomy due to



acute abdomen and it can be the cause of serious abdominal complications. We considered our case interesting because of its rarity and of preoperative diagnosis difficulty.

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# **An Unusual Case of Disseminated Histoplasmosis in an Immunocompetent Patient**

*Elliot Joo, MD, Matthew M. Tsushima, MD, Michael Walter, MD\*.*

*Internal Medicine, Loma Linda University Medical Center, Loma Linda, CA and Gastroenterology, Loma Linda University Medical Center, Loma Linda, CA.*

**Purpose:** Although histoplasmosis in the immunocompetent patient has been reported, dissemination is rare. We report an unusual case of an immunocompetent patient with disseminated histoplasmosis who presented with abdominal pain and bloody diarrhea.

**Results:** A 27 year old Caucasian male with a history of poor oral hygiene presented with tachycardia and daily fevers up to 103°F for nine months following a molar extraction. He initially developed a recurrent oral abscess despite treatment with clindamycin. He then failed to improve with a 10-day course of oral steroids. The patient presented to the emergency room with a temperature of 102.9°F, heart rate of 160/minute. On exam, ulcerated red lesions in the buccal mucosa and gingiva were noted. White blood cell count was  $16.0 \times 10^3/\mu\text{L}$ . The remainder of his blood tests including an HIV test was negative. Blood cultures were drawn and he was started on ampicillin/sulbactam and vancomycin.

The patient was diagnosed with acute necrotizing ulcerative gingivitis and was taken for teeth extraction and debridement. Mandibular biopsy showed findings consistent with osteomyelitis. Biopsy culture was only positive for coagulase negative *Staphylococcus*.

The patient continued to have sinus tachycardia and fevers despite a variety of antibiotic regimens. He then developed abdominal pain and bloody diarrhea. Pseudomembranous colitis was suspected and appropriate treatment was started with no improvement. A colonoscopy revealed numerous ulcerations throughout the colon. Biopsies of the ulcers revealed extensive infiltration with macrophages engorged with *Histoplasma capsulatum*. The previous mandibular biopsy slide was then reviewed and it demonstrated the same organism. Further history taking revealed that the patient was a former resident of Missouri, and had moved to California 3 years ago.

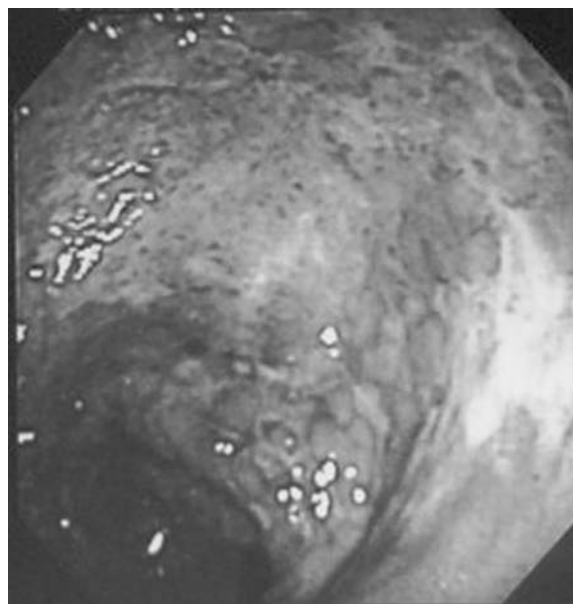
Within several days of starting amphotericin B, his fevers subsided for the first time in nearly 10 months, and his tachycardia markedly improved. He was eventually discharged home with itraconazole.

**Conclusion:** Approximately two-thirds of patients with disseminated histoplasmosis do not have a clear etiology for their hematogenous spread. In our patient, steroid therapy could have led to him being momentarily immunocompromised, promoting hematogenous spread of the fungal spores and consequently, disseminated disease.

A 25 year old healthy woman presented with five days of abdominal pain, nausea, vomiting, diarrhea and haematochezia with a prior upper respiratory tract infection. She denied fever, rash or antibiotic use. Family history was significant for Crohn's disease. Examination showed diffuse abdominal tenderness.

Abnormal laboratory data were: WBC 34 k/cumm, ESR 51 mm/hr, CRP 2.4 mg/dl. The following laboratory data were negative or within normal limits: hb, hct, platelets, BUN, creatinine, urinalysis, serum IgA, IBD serology, ttIgA, stool leucocytes and cultures. Immuno-serological workup was negative. CAT scan of the abdomen showed multiple thickened small bowel loops and edema of stomach and terminal ileum raising possibility of Crohn's disease. Small bowel follow through showed dilated and ulcerated loop of jejunum. Esophagogastroduodenoscopy and colonoscopy were significant for gastritis, erosions and edema of duodenum, sigmoid colon and rectum. Biopsies revealed acute inflammatory changes consistent with immune-mediated vasculitis.

Patient subsequently developed arthralgias and diffuse non blanching petechial rash on the lower extremities. Mesenteric angiogram was normal. Skin biopsy showed leucocytoclastic vasculitis. Immunofluorescence stain showed vascular deposits of fibrin and granular IgA. She was diagnosed with HSP and treated with corticosteroids with remarkable improvement. This case illustrates the potential for diagnostic uncertainty when HSP in adults presents with gastrointestinal symptoms preceding skin manifestations.[figure1]



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# **Henoch-Schonlein Purpura in an Adult Presenting Initially as Acute Gastrointestinal Illness without Skin Manifestations**

*Swetha Kandula, Raymond L. Farrell, Stuart A. Torgerson\*. Division of Gastroenterology, Department of Internal Medicine, Southern Illinois University School of Medicine, Springfield, IL.*

**Purpose:** Henoch-Schonlein purpura (HSP) is a systemic vasculitis that affects small caliber vessels. Patients present with arthralgias, purpuric rash on the lower extremities, and renal involvement. Gastrointestinal symptoms (abdominal pain, nausea, vomiting, diarrhea, bleeding) are more common in children than adults and usually follow skin manifestations. We present a case of HSP in an adult with gastrointestinal involvement documented endoscopically preceding the onset of skin lesions creating a diagnostic dilemma.

811

# **Coil Migration and Cholestatic Jaundice: An Uncommon Late Complication of Hepatic Artery Pseudoaneurysm Embolization**

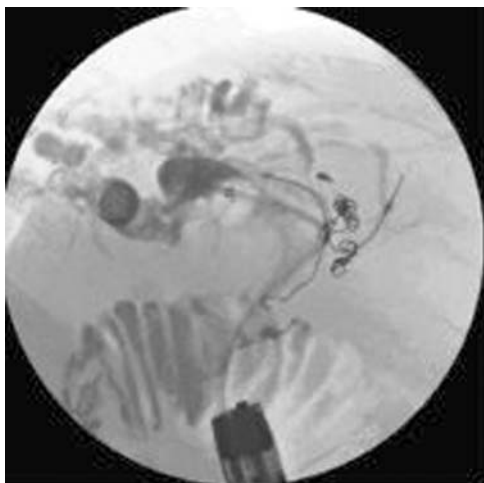
*Rahul Pannala, MD, Baron H. Todd, MD, Vege S. Santhi, MD\*. Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN.*

**Purpose:** 51-year-old White male with neurofibromatosis, and history of pylorus-preserving radical pancreaticoduodenectomy nine years ago for peri-ampullary islet cell cancer and post-operative hepatic artery pseudoaneurysm that was successfully treated by coil embolization presented for evaluation of jaundice. He complained of persistent diarrhea, jaundice and weight loss. Liver chemistries included total bilirubin of 9.2 mg/dL, AST 121 U/L, ALT 119 U/L, alkaline phosphatase of 922 U/L. MRCP revealed marked left hepatic lobar atrophy, intrahepatic bile duct dilatation throughout the left hepatic lobe, several intra-hepatic ductal stones, and changes



suggestive of cholangitis. ERCP confirmed these findings and also noted a partially strictured choledochojunostomy. Balloon dilatation of the choledochojunostomy, extensive stone extraction, and biliary stenting were performed. Repeat ERCP 6 weeks later noted recurrent severe stone burden in the common and left hepatic ducts. Remarkably, a partially uncoiled wire neighboring the right hepatic duct was intraductal possibly causing stricturing and stone formation. The coil was also noted to be intermittently exiting the choledochojunostomy suggesting the possibility that it can be retrieved endoscopically. However, immediately thereafter the patient succumbed to severe cholangitis. Autopsy revealed left hepatic lobar atrophy and a migrated coil in the right hepatic duct.

We report an unusual and previously unreported late complication of coil embolization of a hepatic artery pseudoaneurysm. Our case is unique in the delayed problems from coil migration, the nature of the migration, i.e., into the hepatic duct, and consequent hepatic lobar atrophy, extensive intrahepatic and CBD stone burden with associated stricture of the choledochojunostomy. As pseudoaneurysms do not contain all the layers of the arterial wall there may be an increased propensity for coil erosion and migration. Although ERCP may be the diagnostic method of choice, the present case also highlights that if there is significant stone burden it may be difficult to identify the presence of coils in the hepatic or common bile duct.[figure1]



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### Unusual Pulmonary Complication from Maloney Dilation

David S. Hodges, MD\*, Rishi Raj, MD. Internal Medicine, Texas Tech University Health Sciences Center, Lubbock, TX.

**Purpose:** Complications from bougie dilation of the esophagus are uncommon; most are related to perforation. We describe a case of breakage of Maloney dilator tip during dilation which was silently aspirated and presented with persistent cough.

**Results:** A 70 year old white male presented with intermittent dysphagia to solid food. Upper endoscopy revealed a Schatzki ring at the gastroesophageal junction. Dilation was performed using a 58 French Maloney dilator with minimal resistance. He recovered in the endoscopy unit without incident and discharged home. Late that evening the patient developed dry cough. The cough persisted the following day and patient presented to local minor care center. Localized wheezing was present in right lower lobe; antibiotics were prescribed and patient sent home. Dry cough persisted the next day and patient came to our hospital emergency room. There was no fever, wheezing was audible in right lower lobe. Chest X-ray revealed a 3 cm linear radiopacity in the right lower lobe bronchus, suspicious for a foreign body (Fig. 1). The Maloney dilator used was inspected; the distal tip was missing and corresponded to the length and contour of the suspected pulmonary foreign

body. The patient was admitted; at subsequent bronchoscopy a foreign body was seen and removed from right lower lobe bronchus. Upon inspection, it was the dilator tip (Fig. 2). The patient recovered well with cessation of wheezing and cough. Upon further inspection of our dilators, it was found that the more commonly used dilators had shallow transverse furrows in the tapered tips, resulting from frequent use and disinfectant cleansers. The smaller, less commonly used dilators had no such changes. The complete dilator kit was replaced.

**Conclusion:** Frequently used bougie dilators should be periodically inspected for signs of damage that could result in possible breakage during dilation.[figure1][figure2]



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### Case Series: Lactulose Retention Enema Associated with Massive Gastrointestinal Hemorrhage in Three Patients

William R. Kessler, MD\*. Gastroenterology, Indiana University Medical Center, Indianapolis, IN.

Recently at our institution we observed 3 cases of severe lower gastrointestinal hemorrhage associated with use of the Lactulose Retention Enema (LRE). Practitioners must be aware of the potential complications of using such a device in critically ill, cirrhotic patients.

**Part I:** Chart review, including endoscopic reports, laboratory data, imaging studies and discharge summaries was performed.

**Part II:** Diameter as well as bulb pressure was measured using a retention enema set attached to a manual sphygmomanometer. Once fully deflated the system was closed and measurements were obtained for sequential pumps. This was repeated twice.

**Part I:** During a three month period three patients were identified as having severe lower gastrointestinal hemorrhage associated with the administration of LRE.

**Case 1:** 52 year old male with Hepatitis C Cirrhosis (Child's C) was transferred for management of variceal hemorrhage. LRE was administered for HE. After massive lower gastrointestinal hemorrhage, flexible sigmoidoscopy revealed a 10 cm rectal tear with clot. Patient expired within twenty four hours.

**Case 2:** 51 year old male with Hepatitis C/Alcoholic Cirrhosis (Child's B) was admitted due to Hepato-Renal Syndrome (HRS) and HE. LRE was administered with subsequent massive lower gastrointestinal hemorrhage. Colonoscopy revealed a one-third circumferential rectal tear with clot. Imaging revealed no perforation. Patient survived to discharge.

**Case 3:** 76 year old female with Hepatitis C Cirrhosis (Child's B) was admitted HE following TIPPS procedure. LRE was administered and subsequently massive lower gastrointestinal hemorrhage ensued. Colonoscopy revealed a large rectal mucosal defect and possible ulcer. Imaging revealed no evidence of perforation. Patient survived to discharge.

**Part II:** The mean pressure (mm Hg) and (diameter (cm)) for one, two, three and four pumps was; 107 (4), 195 (4.3), 242 (4.3) and 260 (4.8), respectively (See Table).

Based upon this study we conclude that LRE should be avoided in cirrhotic patients in the critical care setting due to significant morbidity and mortality associated with traumatic complications related to the high intra-bulbar pressures generated in the enema retention system. Our institution favors the use of intravenous antibiotics for HE and has abandoned the practice of LRE.

Pressure and Diameter Measurements

Number Pumps	Mean Pressure (mm Hg)	Mean Diameter (cm)
1	110	4
2	195	4.3
3	242	4.3
4	260	4.8

## 814

### Refractory Peptic Ulcer Disease: A Rare Presentation of Annular Pancreas

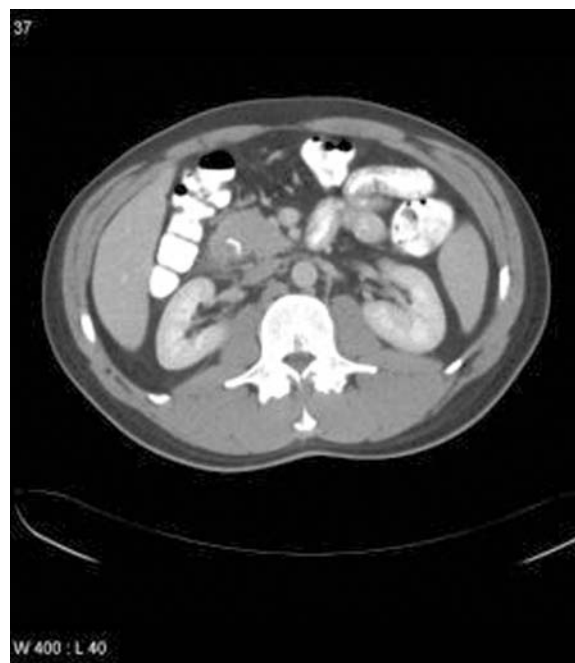
*Laith H. Jamil, MD, Michael C. Duffy, MD, Mitchell S. Cappell, MD, PhD\*. GI, William Beaumont Hospital, Royal Oak, MI.*

**Case:** A 28-year old Caucasian male presented with epigastric pain, nausea, and vomiting. There was no history of NSAID use. He had normal LFTs, amylase and lipase. EGD revealed an ulcerated mass/narrowing in the descending duodenum. Biopsies showed duodenitis, *H. pylori* negative. An UGI series showed a focal constriction in the descending duodenum. Abdominal CT showed an incomplete annular pancreas (AP) encircling the anterior and lateral aspect of the descending duodenum with narrowing of the duodenal lumen. The patient's symptoms initially responded to high dose PPI, but recurred four months later. Repeat EGD showed severe narrowing of the descending duodenum. The patient underwent gastrojejunostomy with relief of the symptoms. Repeat EGD revealed healed ulcers/erosions.

**Discussion:** AP is a rare congenital anomaly (incidence 1:20,000) characterized by a ring of pancreatic tissue surrounding the descending duodenum. It results from failure of the ventral anlage of the pancreas to rotate with the duodenum. There are two main etiologic theories: (1) Lecco's Theory – adherence of the ventral bud to the duodenal wall prior to rotation results in its persistence and encirclement of the duodenum, and (2) Baldwin's

theory – persistence and enlargement of the ventral bud. It can present at any age, including infants. Most adults present between 20 and 50 years of age. Most are asymptomatic. Presenting symptoms include abdominal pain, nausea, postprandial fullness, vomiting, UGI bleeding (from peptic ulcer), acute or chronic pancreatitis, and rarely biliary obstruction. 15% of adults with AP have duodenal stenosis. 33% have PUD. PUD is believed to be due to prolonged stasis of antral contents. The treatment is bypass surgery of the annulus, by duodenojejunostomy, duodenoduodenostomy, or a gastrojejunostomy.

**Conclusion:** This is an unusual presentation of AP in adulthood as a DU and constriction refractory to PPI therapy, which responded to gastrojejunostomy. AP should be strongly considered in the differential diagnosis of a benign idiopathic PUD in the descending duodenum associated with severe focal duodenal narrowing, and refractory to PPI therapy. AP should be excluded by appropriate imaging studies.[figure1]



## 815

### Pyogenic Liver Abscess Complicating Colonoscopic Polypectomy

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Flexible colonoscopy is the "gold-standard" for diagnosis and treatment of colorectal pathology. However, there remain serious, albeit rare, risks of this invasive procedure, including infectious complications.

A 68 year old man with coronary artery disease and diabetes mellitus presented with a three-day history of abdominal cramps, vomiting, and non-bloody diarrhea. The patient had undergone screening colonoscopy one week previously, during which a 2 cm x 3 cm pedunculated polyp was removed from the hepatic flexure using snare cautery. Pathology had revealed a moderately differentiated invasive adenocarcinoma arising in a tubulovillous adenoma.

The patient was febrile to 39 degrees Celsius and physical exam was remarkable for a distended, tender abdomen with decreased bowel sounds. Laboratory studies showed a white blood cell count of 13,400/ $\mu$ L and elevated transaminases to twice the upper limit of normal. Abdominal CT was

obtained, revealing an abscess measuring 8.1 cm in maximum dimension in the posterior segment of the right hepatic lobe. Blood cultures grew *E. coli* and alpha hemolytic streptococci.

The patient was treated with intravenous antibiotics and underwent CT-guided placement of a percutaneous drainage catheter to assist with resolution of the abscess. He ultimately proceeded to right hemicolectomy for resection of the adenocarcinoma.

Presence of colonic tubulovillous adenoma alone, like active inflammatory bowel disease, is considered a risk factor for hepatic abscess development, presumably by causing mucosal defects that allow spontaneous micro-perforation. However, given the brief time-course from colonoscopy to onset of symptoms and location of the polypectomy at the hepatic flexure, we believe our patient's abscess was caused by micro-perforation during the procedure. This case serves to raise our consciousness of the infectious potential of therapeutic colonoscopy, while not diminishing our belief in its power to diagnose and treat gastrointestinal pathology.[figure1]



816

#### Fever of Unknown Origin: Pylephlebitis

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**Background:** Pylephlebitis, or septic thrombophlebitis of the portal vein, is a rare complication of any intraabdominal infectious process that is associated with significant morbidity, including hepatic abscess, bowel ischemia, portal hypertension and death. We describe a case of a patient who presented with fever of unknown origin (FUO), later found to be due to pylephlebitis secondary to clinically silent sigmoid diverticulitis. **Case:** 56 year old male physician presented to an outpatient facility with complaints of fevers, rigors, and myalgia for 5 days. Routine fever work-up revealed a leukocytosis ( $17,300/\mu\text{L}$ ), but negative blood cultures, urinalysis, and CXR. Viral causes were also excluded. High-spiking fevers and rigors continued and empiric antibiotic therapy (levofloxacin) was initiated. Despite treatment, the patient's symptoms persisted for the next 2 weeks and he was subsequently admitted for further evaluation. On admission, his temperature was  $103^\circ\text{F}$ , but physical examination was unremarkable. Laboratory investigations were notable for an increased WBC ( $18,700/\mu\text{L}$ , 90% polys, 17% bands), ESR ( $120\text{ mm/hr}$ ), AST ( $92\text{ IU/L}$ ) and ALT ( $82\text{ IU/L}$ ). Alkaline phosphatase ( $105\text{ IU/L}$ ) and total bilirubin ( $0.5\text{ mg/dL}$ ) were normal, but albumin ( $2.2\text{ g/dL}$ ) was decreased. Abdominal US with dopplers revealed a thrombus in the portal vein and right branch, without signs of portal hypertension, cirrhosis, or collateralization. CT of the abdomen/pelvis with contrast confirmed extensive thrombosis and demonstrated sigmoid diverticulitis. The patient was

placed on broad-spectrum IV antibiotics (piperacillin/tazobactam) and anticoagulation therapy. Admission blood cultures grew anaerobic peptostreptococcus and the diagnosis of pylephlebitis was made. The patient ultimately defervesced and his WBC normalized. His aminotransferases subsequently trended down, and he was discharged on hospital day 6. The patient was to be maintained on long-term IV antibiotic therapy (4–6 weeks of ertapenem) and anticoagulation. An outpatient hypercoagulability work-up, echocardiogram and colonoscopy were all negative. Follow-up CT demonstrated improvement of the pylephlebitis. **Conclusion:** The diagnosis of pylephlebitis should be considered in patients with FUO. Imaging studies are required, not only to demonstrate thrombus, but to identify the underlying source of infection. A high index of clinical suspicion is required in this scenario because aggressive antibiotic therapy can be promptly initiated, avoiding potentially serious complications.

817

#### Pancytopenia in a Patient Treated with 6MP and Fluconazole: A Novel Drug Interaction

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An 83 year old woman with a history of ulcerative colitis was admitted with increased diarrhea and rectal bleeding. Colonoscopy revealed active colitis from the anal verge to the splenic flexure. Prednisone was added to her stable dose of 6 mercaptopurine (6MP). The prednisone was gradually tapered as her symptoms improved. Five months later the patient was readmitted with fatigue and dysphagia. Upper endoscopy revealed white exudates throughout the esophagus consistent with *Candida* esophagitis. Treatment was initiated with oral fluconazole 100 mg daily. The patient's dysphagia improved and she was discharged. Five days later the patient was readmitted with fatigue. A complete blood count revealed a leukocyte count of  $1,600/\mu\text{L}$  with an absolute neutrophil count of  $850/\mu\text{L}$ , hemoglobin of  $8.5\text{ g/dL}$  and platelet count of  $44,000/\mu\text{L}$ . Her baseline leukocyte count ranged from  $4,600/\mu\text{L}$  to  $7,200/\mu\text{L}$ , baseline hemoglobin range;  $10.5\text{ g/dL}$  to  $12\text{ g/dL}$  and baseline platelet range;  $210,000/\mu\text{L}$  to  $300,000/\mu\text{L}$ . Measurements of her 6MP metabolites revealed a 6 Thioguanine (6TG) level of 924 ( $>400 = \text{high risk of leukopenia}$ ) and the 6 methylmercaptopurine (6MMP) level was undetectable. The patient's dose of 6MP was stable and her family verified she had not taken an inadvertent overdose. The fluconazole was discontinued and the hematologic abnormalities resolved over five days.

6MP is metabolized by xanthine oxidase to 6 thiouric acid (6TU). 6 TU is then metabolized by thiopurine methyltransferase (TPMT) to 6TG and 6MMP. Higher levels of 6TG correlate with leukopenia but also with response to therapy. Patients who are homozygous for inactivating mutations of TPMT are at high risk for increased 6TG levels and leukopenia. This patient had tolerated 6MP over many years without developing leukopenia. She rapidly developed leukopenia after the introduction of fluconazole and the leukopenia resolved with the withdrawal of fluconazole. We hypothesize that fluconazole led to a decrease in TPMT activity resulting in high 6TG levels and leukopenia. No previous interaction between 6MP and fluconazole has been described. A significant number of IBD patients receive corticosteroids which puts them at increased risk for fungal infections. Many of these patients may receive fluconazole while concurrently on 6MP. We recommend careful monitoring of the blood count during therapy given the risk of leukopenia in patients receiving 6MP and fluconazole.

818

#### Severe Anemia as the Presenting Feature of Small Bowel Melanoma

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**Introduction:** Melanoma, the most common tumor metastasizing to the GI tract found post-mortem, is rarely symptomatic. Similarly, this cutaneous malignancy is a rare etiology of severe, occult GI bleeding. We report a case of unexplained chronic anemia due to recurrent melanoma in the absence of other suggestive complaints.

**Case Report:** A 70 year-old man with known melanoma diagnosed 3 years previously was sent to the emergency department after routine tests demonstrated severe anemia. Bloodwork was done to prepare for a duodenal biopsy after PET scan for routine metastatic surveillance demonstrated hyperactivity in the duodenum. He gave no history of trauma, bleeding, or GI complaints. Review of symptoms revealed mild fatigue and dyspnea on exertion of unclear duration. Physical exam: blood pressure = 152/90; pulse = 90/minute with minimal postural change. No skin lesions were present. The rest of the exam was unremarkable except stool was positive for occult blood. Hgb. was 6 gm% and iron studies were consistent with a microcytic, hypochromic anemia. Colonoscopy was normal. Upper endoscopy using a pediatric colonoscope demonstrated a 2–3 cm, pigmented, ulcerated mass in the distal duodenum– proximal jejunum. Histology: malignant melanoma. He was referred to medical oncology for treatment options.

**Discussion:** Melanoma is an aggressive tumor; the GI tract is the second most common site of metastasis after the lung. An ante-mortem diagnosis is made in only 1.5% to 4.4% of patients. Diagnostic challenges include (1) small bowel recurrence as late as 21 years after resection of a primary skin lesion, (2) occurrence without a cutaneous site; (3) presentation as a non-pigmented lesion or mimicking a typical benign polyp; (4) non-specific symptoms suggestive of more common disorders. Endoscopically, small bowel lesions manifest as single or multiple mucosal or intramural nodules, ulcerated masses, or as diffuse bowel involvement. This patient underscores the need to consider recurrent, extra-cutaneous tumor in all individuals with a history of melanoma and evidence of GI bleeding of any magnitude. Such patients undergoing endoscopy should have all lesions biopsied to detect possible metastatic disease.

recurrent bleeding over a 3-month period, and the PEG was subsequently removed.

**Discussion:** Percutaneous examination of the ES with contrast was first described by McNeely et al in 1987, and an endoscopic examination with a bronchoscope was first used in 1998. Since then, only few case reports have been published utilizing percutaneous endoscopy to evaluate suspected pathology in the ES. New techniques like double balloon endoscopy have been shown to be useful but the examination may be limited by difficult access, as with our patient. This case highlights the value of percutaneous endoscopy to examine the ES after Roux-en-Y gastric bypass.

## 820

### Rectal Stent Revision Using Argon Plasma Coagulation

Amil Patel, MD, Kamil Obideen, MD\*. *Medicine/Division of Digestive Diseases, Emory University School of Medicine, Atlanta, GA.*

A 66 year old male was referred for evaluation of heme positive stools and constipation. A colonoscopy ultimately revealed an obstructing rectal mass 7 cm from the anal verge (Figure A), and the biopsy was consistent with moderately differentiated rectal adenocarcinoma. A subsequent computed tomography scan and endoscopic ultrasound confirmed a stage IIIB, T3N1M0 rectal adenocarcinoma. A Boston Scientific Wallflex enteral colonic stent size 25 mm × 90 mm was then successfully deployed for symptomatic relief while he underwent neoadjuvant chemoradiation therapy. However, 6 weeks later, the patient began to experience rectal pain, bleeding with bowel movement and intense tenesmus. A repeat flexible sigmoidoscopy revealed that the distal portion of the metal stent was imbedded within the rectal mucosa resulting in irritation (Figure B). Over the course of two subsequent flexible sigmoidoscopies, argon plasma coagulation was utilized at 80 watts

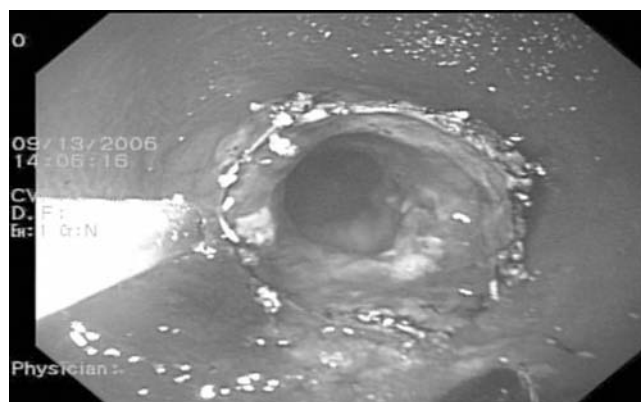
## 819

### Investigation of the Excluded Stomach after Roux-en-Y Gastric Bypass: The Role of Percutaneous Endoscopy

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**Background:** The bypassed portion of the stomach is difficult to access and evaluate after Roux-en-Y gastric bypass. We report a case of obscure gastrointestinal bleeding where successful endoscopic examination of the bypassed stomach and small bowel was made through percutaneous access.

**Case:** A 66-year-old man status post Roux-en-Y gastric bypass surgery for morbid obesity 6-years prior presented to an outside institution with melena and hemodynamic instability. His hemoglobin (Hgb) was 10 gm/dl, a drop from baseline Hgb of 15 gm/dl. The patient was taking aspirin 81 mg daily. Upper endoscopy revealed expected post-surgical changes and colonoscopy showed diverticulosis with no bleeding. A tagged RBC scan revealed a focus of activity in the right upper quadrant. The aspirin was stopped and the patient was discharged following cessation of clinical bleeding and a stable Hgb. He was readmitted five days later with recurrent melena and a Hgb of 8.5 gm/dl. A repeat bleeding scan was negative and capsule endoscopy revealed bleeding at 4 hours into the recording (suspected jejunum). The Roux-en-Y anastomosis was not specifically identified. The patient was transferred to our institution for double balloon endoscopy, but the Roux-en-Y anastomosis was not reached and no proximal source of bleeding was identified. Based on the suspicion that bleeding was coming from the excluded stomach (ES), a percutaneous endoscopy was performed. Once localizing the ES with ultrasound, the stomach was filled with air and a 22 French gastrostomy tube was inserted into stomach with the assistance of fluoroscopy. Through the percutaneous access, we were able to examine the ES and Roux limb to beyond the surgical anastomosis. No source of bleeding was identified, so a button PEG was left in place for future access. The patient experienced no



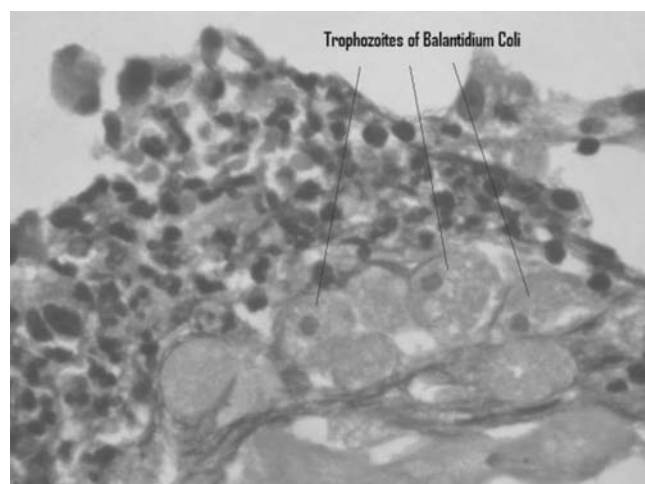
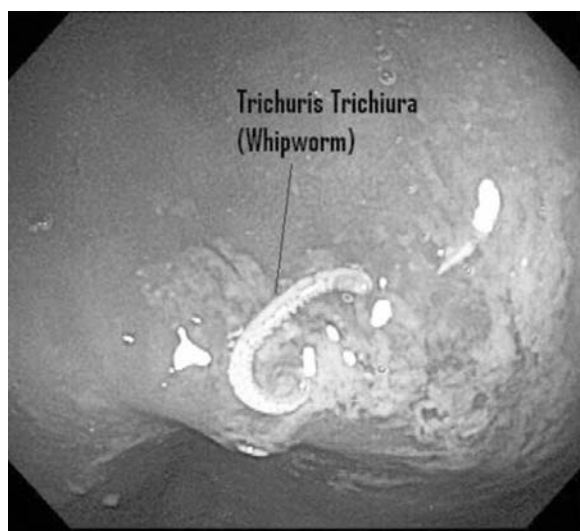
and 0.8 liters/minute to remove the distal portion of the stent and blunt the sharpened edges (C-D). The remnants of the stent were successfully removed using forceps. There was little to no mucosal irritation as a result of the procedure, and the patient's symptoms had dramatically improved at follow-up.[figure1][figure2]

821

### Balantidium Coli and Trichuris Trichiura Co-Infection Presented with Lower Gastrointestinal Bleeding – A Case Report

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*Balantidium coli* (B coli), primarily an intestinal parasite of pigs, is an uncommon protozoan cause of infectious colitis in the United States. Three forms of B coli infection can occur: asymptomatic cyst excretion, acute colitis with prominent bloody diarrhea and chronic infection. We present a case of co-infection with B coli and *Trichuris trichiura* presented as acute colitis. **Case report:** A 46 year-old female from Bangladesh living in Brooklyn, New York for the last 8 years presented with an episode of bloody diarrhea and lower abdominal pain. Her medical history was significant for diabetes mellitus (DM) on insulin therapy. Patient traveled to Bangladesh 6 months ago, stayed at a farm in a remote village and drank water from a well. Physical exam was unremarkable. Laboratory data revealed iron deficiency anemia and uncontrolled DM. Stool studies were negative. Colonoscopy showed



patchy 0.5–0.7 cm discrete ulcers throughout the sigmoid, descending, transverse colon and cecum. A 2 cm live white worm with a whip-like appearance was retrieved from the cecum. Colonic biopsies showed colonic balantidiasis with acute inflammation, superficial ulcerations, inflamed granulation tissue and **trophozoites of balantidium coli**. The worm was identified as **Trichuris trichiura (whipworm)**.

The patient was treated with Albendazole 400 mg daily for 3 days and Tetracycline 500 mg four times daily for 10 days. She had complete resolution of her symptoms and repeated colonoscopy at 6 weeks was normal.

**Discussion:** B coli infection should be considered in patients presenting with bloody diarrhea and history of travel in endemic countries. Patients with other infections or debilitating diseases are more likely to develop symptomatic infections. Co-infection with B coli needs to be considered when other pathogenic parasites are present including nematodes.[figure1][figure2]

822

### The Importance of Belching: Pharmacologic Inhibition of Eructation Presenting as Bloating and Abdominal Pain

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Excessive eructation, or belching, has been looked upon as crass in certain social contexts. Further, this response has been implicated, in part, in the pathophysiology of intractable GERD. Hence, the act of eructation frequently is cast in a negative light. However, the eructation response serves an important role in the alleviation of elevated pressures in the stomach, especially in cases of aerophagia. Here we present an interesting case where the importance of eructation is highlighted, giving rise to a discussion of the mechanism of eructation.

The patient is a 46 year-old male, with a past medical history notable for polysubstance abuse, diabetes mellitus type 2, hypertension, and obesity, admitted to an inpatient medical service for treatment of a septic joint. During his admission, he noted a 2 week history of increasing bloating and transient, sharp epigastric pains. During the same time frame, the patient enrolled in a substance abuse program in which baclofen was initiated and increased. These symptoms totally resolved when made NPO. CT scan of the abdomen and pelvis were negative for any gross pathology, including obstruction, fat stranding, or free air. On exam, multiple bottles of diet carbonated beverages littered the patient's bedside. He admitted to habitually drinking up to 4 L of diet cola a day for the past 2–3 years (preceding the initiation of baclofen). Upon cessation of carbonated beverages, the symptoms completely resolved. However, since the patient refused to continue abstinence of carbonated beverages, the dosage of the baclofen was slowly titrated down. With the removal of the baclofen, the patient was able to continue his habit without symptoms.

Ingested carbonated beverages elaborate a large amount of gas in the stomach. When gastric intraluminal pressures are high due to ingested air, the rate of transient lower esophageal relaxations (TLESR) increases, leading to the eructation response. It has been shown that baclofen, a GABA(B) receptor agonist, inhibits TLESRs by modulating gastric mechanoreceptor and CNS-Vagus nerve transduction. Hence, when baclofen was started, the patient's eructation response was inhibited, leading to increased gastric pressures and, presumably, the described symptoms. Discontinuation of the baclofen allowed for return of the proper stimulation of TLESRs and eventual alleviation of the patient's pain.

823

### Autoimmune Pancreatitis (AIP) – A More Younger and Diverse Disease

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AIP was first proposed as a distinct entity of chronic pancreatitis in 1995. The incidence, prevalence and clinical characteristics worldwide are yet being investigated. Common age of presentation is between of 45–75 years with a distinct male predominance.

We present a 23-year-old African American, HIV + obese male (BMI 47.5) with one week of painless jaundice, unintentional 20 pound weight loss in the last 3 months and symptoms of cholangitis 24 hours prior to admission. Liver chemistries revealed elevation with clear cholestatic pattern: Direct hyperbilirubinemia (22 mg/dl) alkaline phosphatase more than three times upper normal limit, normal transaminases, inversion of the albumin to globulin ratio. Pancreatic enzymes were normal as well as electrolytes and glucose. Liver ultrasound showed intra and extra hepatic ductal dilatation. Triple phase CT of the pancreas revealed a diffusely enlarged pancreas without phlegmonous changes, calcification, or pseudocysts and a narrowed, irregular pancreatic duct. The arterial enhanced images demonstrated a hypo dense pancreas with increased peripheral attenuation in delayed phase. Traditional auto-immune markers were negative except for a weakly positive SMA (1:20). Total serum Gammaglobulins were elevated with IgG Subclass 4 normal. CD4 count was normal.

ERCP identified a smooth, 4 cm distal common bile duct stricture. A percutaneous pancreatic biopsy confirmed the diagnosis of sclerosing lymphoplasmacytic pancreatitis. Treatment with oral prednisone at 40 mg/ day led to rapid normalization of liver chemistries and full cholangiographic resolution of the stricture. This case illustrates that AIP is not limited to the older age group and can be seen in younger African American patients.

This is the first reported case of AIP in a patient with HIV. Whether this is a chance association is unclear and will need to be looked at with further reports of this interesting disease.

## 824

### Gastrointestinal Stromal Tumor and Papillary Renal Cell Carcinoma: A Case Report

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There are only 4 reported cases of GIST found with concomitant PRCC. A 50 y o male with HTN presented after a presyncopal episode, with dizziness, and black stool for 1 month. PE remarkable only for melena. Iron deficiency anemia was seen on labs, large hiatal hernia on EGD and a normal colonoscopy. A 9 × 5 cm right pelvic mass was seen on CT scan with a meniscal sign of the oral contrast suggesting ileal neoplasm (Fig. 1), and a 5 × 4 cm right kidney mass. Laparoscopic excision of a 6 × 8 cm ileal tumor showed malignant GIST, with spindle cells, vesicular nuclei and a 5/50 hpf mitotic rate. Histochemical staining was positive for CD117. CT guided biopsy of the renal mass showed PRCC. The patient underwent a total right nephrectomy without post-op chemotherapy. GISTs are differentiated from other smooth muscle neoplasms by the identification of the CD117 antigen on immunohistochemical staining. CD117 is part of the c-kit receptor, a membrane tyrosine kinase and a product of the c-kit or KIT proto-oncogene. Other non-GIST spindle cell neoplasms of the GI tract do not carry this mutation, which is clinically relevant because the c-kit mutation is sensitive to imatinib, a selective tyrosine kinase inhibitor. Surgical resection is the treatment of choice, but only half are recurrence free for five years. Imatinib is successful as adjuvant therapy in advanced disease and an option for unresectable disease. Both PRCC and GIST have been connected to mutations in the proto-oncogenes c-MET and c-KIT however this association is only seen in recurrent familial tumors, not sporadic as seen in this patient. A case report describes a patient with metastatic GIST and PRCC, treated with imatinib. Six months later, all hepatic lesions had regressed.

However, the renal masses increased in size, raising questions regarding the effect of imatinib for treatment of GIST on PRCC. In this situation, perhaps sunitinib should be considered as first-line treatment as it has been FDA-approved for treatment in imatinib refractory patients with GIST and in patients with advanced renal cell carcinoma.[figure1]



## 825

### Autoimmune Cholangitis in a Patient without AIP

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A 42 year-old male, presents with fatigue, pruitus, 20 lb weight loss and RUQ discomfort. Laboratory data is shown in Figure 1. MRCP revealed a 9 mm focal stricture at junction of CHD & proximal CBD. The typical beaded appearance of PSC was not noted. Liver biopsy revealed patchy lobular and portal chronic inflammation without cirrhosis. Treatment included prednisone and ursodiol. Following therapy, the patient clinically improved. After the steroids were discontinued he again became symptomatic. Table 1 shows the trend of liver enzymes, IgG and CRP levels throughout the treatment course.

Table 1.

Tx	Alk-phos	IgG	IgG4	CRP
Pre Tx	881	2297	210	—
Pred40 mg	382	1500	114	2.0
Off Pred	316	2192	189	3.2
Pred30 mg	263	1620	129	2.0

**Discussion:** AIP is characterized by an inflammatory process in which prominent lymphocyte infiltration with associated fibrosis of the pancreas causes organ dysfunction. The current diagnostic criteria is based on the Japanese criteria including: 1) narrowing of >1/3 of the pancreatic duct on ERCP as well as enlargement of the pancreas; 2) elevated levels of serum IgG4 or the presence of autoantibodies, and 3) evidence of lymphoplasmacytic changes within the pancreatic parenchyma on biopsy<sup>1</sup>. Biliary strictures may be present as diffuse monomorphic or long segmental strictures of the intrapancreatic portion of the CBD, irregular narrowing of the extrahepatic bile ducts and less frequently, enlarged intrahepatic bile ducts<sup>2</sup>. Patients with SC typically associated with AIP have a better prognosis than classic PSC patients. Both SC and pancreatic lesions respond well to steroids and in some cases, stenting<sup>3</sup>. <sup>1</sup>Japan Pancreas Society. Diagnostic Criteria for AIP 2002. Journal of Japan Pancreas Society 2002;17:585–7. Dmitry et al; AIP, NEMJ 2006; 355: 2670–6. <sup>3</sup>Takahiro Nakazawa, MD, et al, Clinical Differences Between Primary Sclerosing Cholangitis and Sclerosing Cholangitis With AIP.

826

### Isolated Histoplasma Colitis Masquerading as Idiopathic Inflammatory Bowel Disease

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To recognize histoplasma infection as a cause of gastrointestinal bleeding and colitis in high risk subjects.

A 41 year old BW presented to UAMS Medical Center for evaluation of fatigue, low grade fever, abdominal pain and bloody diarrhea of 3 weeks duration. Physical exam showed a well nourished lady in no apparent distress. Abdomen was mildly distended with diffuse tenderness to palpation, without guarding or rebound. Rectal exam revealed hemocult positive red-dish brown stool. Labs revealed H/H 5.3/17.7. LFT, BMP, PT/ INR were within normal limits. Stool studies for leucocytes, ova and parasites and *C. difficile* were negative. After initial stabilization, upper and lower GI endoscopy was performed. EGD was normal, and colonoscopy revealed diffuse erythema with clean based ulcers at the hepatic flexure and transverse colon. Histopathology revealed active colitis. Bloody diarrhea subsided and she was discharged on oral Metronidazole and Mesalamine.

Two months later, she returned with worsening abdominal pain, fever and hematochezia. CT of the abdomen showed a thickened ascending colon and parts of the transverse colon. Repeat colonoscopy showed several superficial mucosal ulcerations scattered throughout the ascending and transverse colon. Gomori-methenamine-silver stain (GMS) of the biopsy revealed numerous yeast forms, consistent with histoplasma infection. Urinary antigen for Histoplasma was strongly positive. Cultures from the specimen were positive for *Histoplasma capsulatum*, confirming the diagnosis. Treatment with liposomal amphotericin B and Itraconazole was initiated. On follow up visit she remained symptom free. **Clinical manifestations** of gastrointestinal histoplasmosis range from asymptomatic to nonspecific like nausea, vomiting, diarrhea and abdominal pain. Colonic involvement can be the first clinical sign of disseminated histoplasmosis. The terminal ileum and cecum are the most commonly involved. Ulcers are the most common lesions. Typically ulcers appear as annular shaped lesion with raised borders and necrotic base. Other lesions include mucosal erythema, nodules, polyps, hypertrophied folds and Mass lesions. **Detection** of histoplasma antigen in the urine is a rapid method of diagnosis. Direct microscopic examination of clinical specimen stained using GMS aids in rapid diagnosis. Amphotericin B is the appropriate initial Treatment. Itraconazole 200 mg once or twice daily for 6 to 18 months is used for maintenance therapy.

827

### Advanced Liver Disease in a Patient with PiMZ alpha-1 Antitrypsin (A<sub>1</sub>AT) Phenotype and Normal Serum A<sub>1</sub>AT Level

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A 23 year old woman with a history of diabetes mellitus since age 12 and incidentally-noted thrombocytopenia was seen for recurrent abdominal pain and was found by abdominal ultrasonography to have splenomegaly with prominent vascularity in splenic hilum. An abdominal CT confirmed marked splenomegaly and revealed a small lobulated liver and vascular structures suspicious for abdominal collaterals. She denied icterus, jaundice, pruritis, rash, confusion, sleep abnormalities, fatigue, poor appetite or weight loss. She also denied alcohol use, injection drug use, cocaine snorting or blood transfusions, but had some tattooing 2 months ago.

Physical examination revealed bronzing of skin, spider nevi, and a systolic ejection murmur. Abdominal was soft and protuberant. The liver tip could not be appreciated, the spleen was enlarged and there was no shifting dullness.

Laboratory studies: WBC 3200, platelets 48,000, albumin 3.6 g/dl, AST 53 U/L, ALT 36 U/L, total bilirubin 2.4 mg/dl, direct bilirubin 1.2 mg/dl, alkaline phosphatase 780 U/L, and GGT 1538 U/L. Further workup included normal ceruloplasmin, iron studies, A<sub>1</sub>AT and alpha-fetoprotein, and was negative for viral (A, B and C) and autoimmune hepatitis, raising the possibility of NASH.

A liver biopsy revealed cirrhosis with PAS-positive inclusions in hepatocytes and minimal steatosis. A<sub>1</sub>AT phenotyping revealed MZ phenotype. Subsequently, she developed ascites and was worked up for liver transplantation. A<sub>1</sub>AT is a protease inhibitor (Pi) secreted predominantly by the liver and its deficiency leads to liver disease in a small percentage of patients due to intracellular retention of the mutant protein. Several mutant alleles involving a single amino acid substitution have been identified. PiZZ homozygosity is most commonly associated with A<sub>1</sub>AT deficiency and involves accumulation of mutant A<sub>1</sub>AT in the liver in PAS-positive globules. Although patients carrying a single Z allele (Pi\*Z) have been reported to be at a higher risk of developing cirrhosis, the role of PiMZ in the development of advanced liver disease is not widely known. This case highlights the importance of considering PiMZ phenotype in patients with normal A<sub>1</sub>AT level presenting with liver disease of unclear etiology.

828

### HIV-Associated Non-Hodgkin's Lymphoma of the Small Intestine

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The diagnosis of small bowel tumors is often difficult due to the rarity of these lesions, and the nonspecific and variable nature of the presenting signs and symptoms.

A 59 year old white male with a history of HIV \ AIDS (CD4 = 73) who presented to the hospital with 1 week history of generalized weakness, poor oral intake, non productive cough and mental status changes. He denied any fever, chills, dyspnea, or GI complaints.

His initial work up demonstrated WBC 16.7 (Neutrophils 25%, Bands 8%, and Lymphocytes 22%), thrombocytopenia (29000), anemia (Hgb 11.8 g/dl), and elevated LFTs (Ast 175 U/L, Alt 98 U/L, Bilirubin 1.1 mg/dl, Alkaline phosphatase 1078 U/L).

He had Head CT scan which was unremarkable, abdominal U/S which revealed fatty liver with two liver cysts in the right lobe and splenomegaly, and abdominal CT scan which showed 9 cm mass like mural thickening involving the terminal ileum, moderate retroperitoneal and abdominal lymphadenopathy, splenomegaly, and small ascites.

Colonoscopy was done which showed an exophytic bulky mass in the terminal ileum extending to the ileocecal valve with friable overlying mucosa. Biopsies showed Non Hodgkin's lymphoma – B cell type. The Bone marrow biopsy demonstrated bone marrow diffusely involved by non Hodgkin's lymphoma. Patient became hypoxic and more confused, the family refused any further investigations or treatments and he expired two days later.

**Discussion:** Small bowel malignancies account for only 2–3% of all gastrointestinal (GI) neoplasms, and less than 0.4% of all cancers in the United States. Primary GI lymphoma is the most common extranodal form of lymphoma; the stomach (75%) and small bowel (9%) are most often involved. Small bowel lymphoma occurs predominantly in male adults, peaking in the seventh decade. Most tumors are focal and involve the distal small intestine. The incidence of primary intestinal lymphoma in the United States doubled between 1985 and 1991. Among the factors implicated in this increase is the increasing number of immunocompromised patients (eg, AIDS, transplantation recipients), and the increasing immigration from Third World countries.

829

### Ischemic Liver Insult in a Patient with Sick Beta Thalassemia 0: First Reported Case



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A 34 years old African American lady with a past medical history of Sickle Beta Thalassemia 0 (hemoglobin electrophoresis revealed a hg A1:0%, A2: 3.2%, S: 73.2%, F: 23.6%), Hepatitis A Exposure and immunity, and hypertension who presented with jaundice and right upper quadrant abdominal discomfort. She was not on any known hepatotoxic medications and there was no history of either hypotension or cardiac dysrhythmias. Physical examination showed a normal blood pressure, significant jaundice, no sign of encephalopathy, a normal liver size with no stigmata of chronic liver disease. Complete blood count revealed hemoglobin of 11.5 g/dL, hematocrit of 33%, WBC 4.9 and Platelet of 134,000. Liver function test showed an INR 1.1, AST 1519, Alt 1413, Alkaline phosphatase 158, total bilirubin 5.6 and conjugated bilirubin of 3.9, LDH 697. Further serological investigation included a negative anti-mitochondrial and anti-smooth muscle antibodies. Her jaundice worsened and further radiological investigations including an ultrasound and a CT scan of the Abdomen revealed a homogenous liver with an irregular contour along the anterior aspect of the right lobe of the liver. These were followed by an MRI/MRA of the liver, which reported capsular retraction with abnormal signal enhancement in the anterior aspect of the liver. Later, a diagnostic liver biopsy disclosed the presence of ischemic hepatitis with marked congestion, fibrosis and presence of sickled cells within dilated sinusoids.

Liver involvement is common in Patients with Sickle cell disease. Hepatic lesions in sickle cell disease have been reported in many patterns consisting of sinusoidal dilatation, perisinusoidal fibrosis and acute ischemic necrosis. However, Sickle Beta Thalassemia 0 is known to have a relatively/comparatively benign course in relation to severity and frequency of vaso-occlusive crises. This case is particularly unique for significant ischemic hepatitis in a patient with Sickle Thalassemia 0, which is yet to be described in the literature.

## 830

### Endoscopic Management of a Large Pancreatic Duct Stone

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**Background:** Pancreatic duct stones (PDS) are found in approximately 35% of patients with chronic pancreatitis. Large PDS can lead to obstructive pancreatopathy and consequent recurrent attacks of pancreatitis. Endoscopic extraction of large or complicated pancreatic duct stones have routinely yielded mediocre results. Extracorporeal shock wave lithotripsy (ESWL) has demonstrated efficacy as a salvage therapy in such patients who are not surgical candidates. We report a case of a large pancreatic duct stone extraction utilizing endoscopic therapy in conjunction with ESWL obviating the need for surgery.

**Case:** A 34-year-old woman was referred for the evaluation and management of idiopathic acute recurrent pancreatitis. An endoscopic ultrasound (EUS) was performed revealing changes consistent with chronic pancreatitis, incomplete divisum, and a 2.7 × 1.9 cm stone in the ventral pancreatic duct (Wirsung). The patient underwent two attempts of Endoscopic Retrograde Cholangiopancreatography (ERCP) yielding unsuccessful pancreatic duct cannulation due to impaction of the stone at the pancreatic orifice. A few months later she presented to our institution with another bout of acute on chronic pancreatitis prompting surgical evaluation for decompression surgery. Alternatively, the patient underwent ESWL using a Medstone STS-TC Shock Wave Generator with 2400 shocks at 20 KV directed at the radio opaque stone in the RUQ. Post ESWL, cannulation of the pancreatic duct was achieved revealing a tight stricture in the head with a downstream 2.5 cm stone. Despite performing a pancreatic septotomy, balloon dilation of the stricture and mechanical lithotripsy we were unable to extract the stone. Two

5 Fr/5 cm pancreatic duct stents were then deployed in the ventral duct. A second course of ESWL with similar settings was then performed directed at the stents. On follow up ERCP, the pancreatic stents were removed. The pancreatogram revealed small fragments of stone in the ventral duct which were easily extracted with a balloon. The patient has been pain-free during her fourth month of follow up with no recurrent bouts of pancreatitis.

**Conclusion:** ESWL in conjunction with endoscopic therapy is a safe and effective approach for large or complicated pancreatic duct stones and should be considered early in the management of this entity.

## 831

### EUS Guided Diagnosis of New-Onset Sarcoidosis in a Patient with Cervical Cancer

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**Case:** A 36-year-old Hispanic woman with squamous cell cervical cancer, stage IIIB, presented to the emergency department with pleuritic chest pain, a persistent non-productive cough and new-onset dyspnea-on-exertion for 5 days. She denied dysphagia, odynophagia, abdominal pain, fever, night sweats, hemoptysis or hematemesis. Social, family, and travel history were non-contributory. Review of systems was positive for 10 pound weight loss in 4 months.

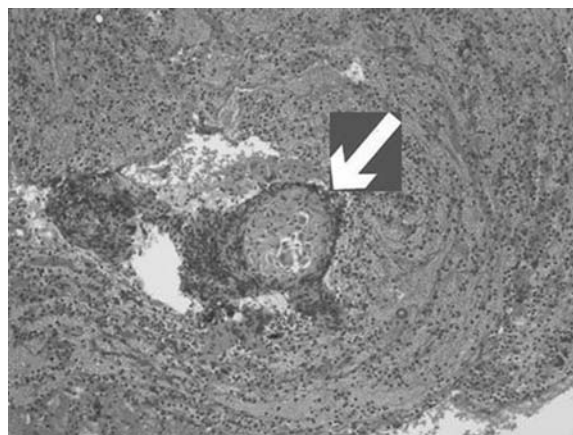
Physical exam only revealed tachycardia and fine basilar rales in the posterior lung fields.

Initial lab data showed: Hb 8 (12–16 g/dL), MCV 73 (80–100), Iron 53 (65–175 ug/dL), and ACE level of 77(12–68 u/L). SMA 7, liver tests, and coagulation profile were normal. HIV serology was negative. CT chest demonstrated mediastinal lymphadenopathy. A PET scan showed intense mediastinal lymph node uptake suggestive of metastatic disease. An endoscopic ultrasound (EUS) was subsequently performed to make a definitive diagnosis.

EUS of the mediastinum revealed a large hypoechoic subcarinal lymph node with irregular borders. EUS-guided fine needle aspiration (FNA) was negative for malignant cells but showed scattered non-caseating granuloma consistent with sarcoidosis (Figure 1). Steroid therapy was initiated which resulted in significant symptomatic and radiographic improvement.

**Discussion:** EUS-FNA was first proposed as an accurate and simple diagnostic modality for sarcoidosis in 1999. Since then, several studies have demonstrated the efficacy of EUS-FNA in obtaining a definitive diagnosis in patients with mediastinal lymphadenopathy.

Despite these promising reports, EUS-FNA currently is underused for definitive diagnosis of mediastinal lymphadenopathy. We report a case which demonstrates the clinical utility of EUS-FNA as a diagnostic modality in a woman with cervical cancer and new-onset sarcoidosis.[figure1]





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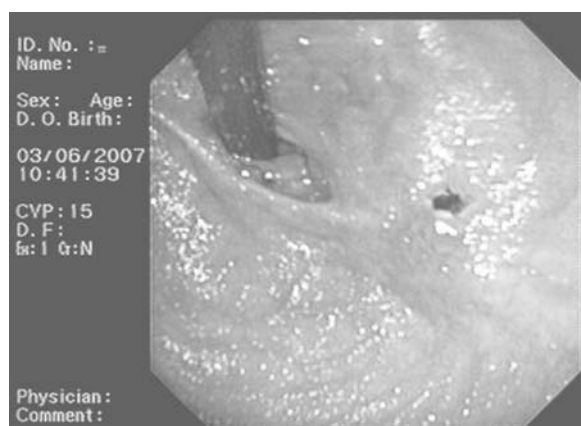
**The Koch Pouch Revisited: Traumatic Ulcerations in a Koch Pouch**

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The Koch pouch, invented by Dr. Nils Koch in the late 1960s, was the first type of continent ileostomy. It was created to provide a better lifestyle for patients who had to have their colons removed for treatment of colitis and other diseases. Its popularity has decreased over time, due to the fact that it is a technically demanding construction and sometimes associated with complications. We describe a case of a patient with a Koch pouch who was found on endoscopic examination to have complications associated with the management of his pouch.

This is a 64 year-old man who had a Koch continent ileostomy for ulcerative colitis in 1975. He inserts a catheter through his one way nipple valve to empty his pouch six to seven times a day. He has been feeling well and denies any gastrointestinal complaints. He presents for annual dysplasia surveillance of his pouch.

On exam, he is afebrile and vitals are stable. His nipple valve on the right side of his abdomen appears unremarkable, without signs of infection. The patient is brought to the endoscopy suite and medicated for moderate sedation. A gastroscope is inserted through the valve orifice. The general mucosa of the pouch appears unremarkable. However, advancement of the scope to the distal end of the pouch reveals several clean-based ulcers in close proximity to each other (see Figure 2). These are attributed to traumatic injury from the patient's frequent catheterizations. Retroflexion reveals a narrowed, but patent, lumen of the afferent limb (see Figure 2). Surveillance biopsies of the pouch are negative for dysplasia.[figure1][figure2]



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**Laser Lithotripsy for Removal of a Difficult To Treat Common Bile Duct Stone: A Collaborative Effort among Gastroenterology, Urology, and Radiology Departments**

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Laser lithotripsy is being increasingly utilized to remove difficult to treat common bile duct (CBD) stones. These procedures are usually performed at referral centers that have the equipment and volume of patients to perform these procedures. We describe a case of a patient with a retained CBD stone that failed multiple types of treatment, but was finally dissolved through a collaborative effort of the departments of Gastroenterology, Urology, and Radiology.

This is a 58 year-old man with a history of cholelithiasis for thirty years. Eleven months ago, he was admitted to an outside hospital for febrile jaundice. An ultrasound revealed intra- and extrahepatic duct dilatation, several small stones in the cystic duct and a large stone in the CBD. Endoscopic retrograde cholangiopancreatography (ERCP) restored some flow in the CBD, but the CBD stone remained. He was scheduled for a repeat ERCP to attempt to remove the stone again, but he was lost to follow-up. Five months ago, he underwent a cholecystectomy, and was found to have a trapped CBD stone. An attempt by the surgeon to remove the stone through the percutaneous transhepatic drain was unsuccessful. The patient then came to our institution and had an ERCP with extension of the sphincterotomy. However, attempts to remove the stone with a trapezoid basket were unsuccessful. Next, extracorporeal shock wave lithotripsy (ESWL) was performed, but without apparent fragmentation of the CBD stone. Finally, it was decided to perform laser lithotripsy.

The gastroenterologist, urologist, and radiologist, working in collaboration, performed a percutaneous laser lithotripsy. Cholangiogram through the biliary catheter revealed a large CBD stone approximately 2 cm in size. With the guidance of fluoroscopy, a ureteral access catheter was inserted over a wire into the CBD. A ureteroscope was advanced into the CBD to the level of the stone. A 200 micron holmium laser fiber was used to perform lithotripsy. Pulverization of the stone was confirmed through a contrast study.

**Discussion:** We demonstrate a case of successful laser lithotripsy on a difficult to remove CBD stone through a collaborative effort of Gastroenterology, Urology, and Radiology. Using this model, laser lithotripsy may be performed successfully not only in referral centers, but in community-based hospitals as well.

834

**Improvement of Cardiomyopathy after Infliximab Treatment for Crohn's Disease (CD)**

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Rare instances for cardiovascular complications of Inflammatory Bowel Disease have been reported, including valvular insufficiency, conduction disorders, pericarditis, myocarditis, pericardial tamponade, dilated cardiomyopathies (DCM) and endomyocardial fibrosis. Caution has been advised when using infliximab (INF) in patients with heart disease, especially DCM, because of an increased risk of sudden death.

We report a 17 y/o male with CD diagnosed at 9 yrs age, when he presented bloody diarrhea, weight loss and abdominal pain. He had many hospitalizations for exacerbations and perianal fistulizing disease treated with courses of steroids and 5-ASA. In 2004, progressive shortness of breath leading to mechanical ventilation prompted a diagnosis of DCM, with ejection fraction (EF) of 22%. Treatment with carvedilol and ACE inhibitors stabilized his heart disease. In 2005, he developed a retroperitoneal abscess requiring drainage and antibiotics. An colocutaneous fistula required a segmental colectomy with end colostomy and mucous fistula. In early 2006, he

presented with an acute abdomen. Exploratory revealed a jejunal volvulus with necrosis and severe colonic disease, requiring segmental small bowel resection, subtotal colectomy and end ileostomy. Because of the aggressive disease, infliximab therapy was considered. EF was 36%. With close cardiac monitoring, IFX at 5 mg/Kg for a dose of 170 mg/infusion was started. Induction therapy was completed uneventfully, and 2 months later he had gained 10 lbs, steroids were discontinued, perianal fistula had closed, and EF 46%. IFX dose was adjusted by weight. By 6 months, he had 25 lbs and EF was 56%. He has continued doing well on maintenance IFX and azathioprine.

Complications of the cardiovascular system by Crohn's disease are uncommon. Most of the reported complications related to CD are myocarditis and pericarditis but dilated cardiomyopathy has been described. Vasculitis is part of the pathological spectrum of inflammatory bowel disease and the most probable mechanism for cardiovascular injury. We successfully treated a patient with CD and DCM with improvement of systolic function and clinical status. We wonder whether his DCM is an undiagnosed manifestation of CD or an unrelated complicating illness.

835

#### **Vaginal Crohn's Disease Successfully Treated with Adalimumab**

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The patient is a 36 year-old woman with a 15-year history of colonic and perianal Crohn's Disease (CD) complicated by rectovaginal fistula, status-post a total proctocolectomy with end-ileostomy in 2004 for medically-refractory disease, including incomplete responses to infliximab and cyclosporine. The patient enjoyed a surgically-induced remission until May 2006, when she developed vaginal pain, swelling, and ulceration; she had no gastrointestinal symptoms, fevers or weight loss but was fatigued and had left knee swelling and pain. Physical exam was notable for diffuse edema, induration, ulcers and mucopus of the vaginal introitus, labia minora, and inner labia majora in addition to left knee suprapatellar tenderness, edema and small effusion. Laboratory tests were significant for Hgb 5.9 g/dL, ferritin 6 ng/mL, and CRP 3.9 mg/dL. Herpes simplex, Haemophilus ducreyi, and AFB cultures were negative as were Chlamydia, RPR and HIV serologies. Vaginal biopsies revealed dense, diffuse mixed inflammation with multinucleated giant cells and granulomas consistent with CD; special stains for fungi and bacteria were negative. Pelvic MRI showed vaginal distention, thickening and a possible fistula from the posterior inferior vagina to the perineal soft tissue. Small bowel series was normal. Knee aspiration was consistent with an inflammatory effusion. A diagnosis of vaginal CD with early fistula and peripheral arthropathy was made. She was transfused packed RBCs to a Hgb 10.3 and treated with intravenous steroids and antibiotics with no improvement. She was subsequently enrolled in an open-label adalimumab study for patients with previous infliximab exposure (the CHOICE trial): she received an induction regimen with 160 and 80 mg subcutaneously at 0 and 2 weeks, followed by 40 mg every other week. She was started on concomitant 6-MP 50 mg/day. Within 1 week, she reported markedly decreased vaginal and knee symptoms. Six weeks after starting treatment, exam revealed nearly normal vaginal mucosa, with only 2 small ulcer scars. Her knee edema and effusion had resolved, and her Hgb was stable without further transfusions. She has remained well on maintenance adalimumab every other week for 7.5 months. This case is the first known report of successful treatment of mucocutaneous vaginal CD with adalimumab.

836

#### **An Unusual "PPI-Refractory" Symptomatic Gastric Ulcer Successfully Treated with Corticosteroids and Azathioprine: Eosinophilic Mural Ulcer**

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MD\*. Internal Medicine/GI, University of Illinois, Advocate Christ Med Ctr, Chicago/Oak Lawn, IL.

A 23-year-old female was evaluated for chronic abdominal pain and iron deficiency anemia. She was initially diagnosed with peptic ulcer disease and was treated with a proton pump inhibitor (PPI). An initial upper endoscopy demonstrated a large antral gastric ulcer. Biopsy showed mixed inflammatory cell infiltration and no Helicobacter pylori organisms were seen. However, she continued to have rather severe epigastric pain requiring narcotic analgesics despite continuous aggressive therapy with a PPI. Past medical history included asthma. Physical examination was unremarkable except for epigastric tenderness. Laboratory studies showed a hemoglobin of 8 g/dL, MCV 69 fL, white blood cell count 6,100/uL with 11% eosinophils. Abdominal imaging studies looking for other causes of her pain were negative. The possibility of noncompliance with PPI treatment or OTC NSAID use was raised. However, repeat endoscopy in June 2007 revealed a larger prepyloric penetrating ulcer and an adjacent smaller antral ulcer. Multiple biopsies were obtained and demonstrated abundant eosinophilic infiltration. Serum gastrin was normal. Colonoscopy was unremarkable. The diagnosis of eosinophilic mural gastric ulcer was made and she was started on prednisone 50 mg daily concomitantly with Azathioprine 50 mg to be increased to 100 mg daily in addition to a proton pump inhibitor. Dramatic symptomatic and clinical improvement occurred shortly after medical therapy was initiated. Eosinophilic gastric ulcer is believed to be a rare/localized manifestation of the entity of eosinophilic gastroenteritis. This case uniquely illustrates (1) a refractory large, gastric ulcer with a smaller adjacent ulcer. (2) clinically manifesting as persistent problematic upper abdominal pain and iron deficiency anemia, and (3) immediate improvement with corticosteroid/immune modulator therapy without the need for surgical intervention. Clinicians and Gastroenterologists should suspect this readily treatable entity in cases of ulcers with unusual clinical behavior.

## **OUTCOMES RESEARCH**

837

#### **Proton Pump Inhibitors vs. Histamine2 Receptor Antagonist in Treatment of Non Variceal Upper Gastrointestinal Bleed: A Meta-Analysis**

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**Purpose:** To evaluate whether proton pump inhibitors (PPI) are more effective than histamine2 receptor antagonist (H2RA) in treatment of non variceal upper gastrointestinal bleed (UGI) and to compare the impact on mortality, rate of rebleed, surgical intervention, length of stay and need for transfusion. UGI bleed is a frequent problem in United States with an annual incidence of 100 per 100,000. Randomized control trials on UGI bleed have conflicting results and are heterogeneous with above mentioned outcomes.

**Methods:** Metanalysis of comparative randomized control trials of PPI vs. H2RA in non variceal UGI bleed from 1990–2006 using Pubmed, Medline, Embase databases. The included trials indicated one of the outcomes as mortality, rebleed rate, surgical intervention, length of stay or transfusion requirement. Two reviewers independently reviewed a total of 31 trials with 3,846 patients. These trials fulfilled the inclusion criterion and contained data for atleast one of the outcomes.

**Results:** Recurrent bleed was noted in 7.3% (95% CI 5.5–9.2) of patients treated by PPI vs. 13.9% (95% CI 11.4–16.3) of patients treated with H2RA (OR 0.5 95% CI 0.42–0.69). Surgical intervention was needed in 4.8% (95% CI 2.9–6.0) of patients treated with PPI vs. in 7.1% (95% CI 5.2–9.3) of patients treated with H2RA (OR 0.6 95% CI 0.50–0.84). Mortality as an endpoint was seen in 1.8% (95% CI 0.9–3.1) patients treated with PPI vs. 2.5% (95% CI 1.5–3.9) in patients treated with H2RA (OR 0.71 95% CI 0.59–2.10). 21% of patients treated with PPI required blood transfusion (95% CI 16.2–26.9) vs. 29% of patients (95% CI 24.7–32.0%) treated with H2RA



contrast to teleconferences (N = 7, 7%). The majority of respondents (N = 75, 74%) prefer face-to-face interaction while only 28% prefer web-based learning. Driving distance to programs does not appear to be a major barrier to attendance as 71% (N = 72) are willing to travel > 10 miles. Wednesday (N = 38, 38%) & Saturday (N = 43, 43%) are the most preferred days. Evening (N = 57, 56%) is the preferred time for live programs with the start time of 7 p.m. (N = 48, 48%). Those who prefer Saturday favored morning programs, 30% (N = 30) desired programs two hours in length, & 39% (N = 39) favored a program half-day in length. 64% (N = 65) of responders felt CME credits were either important or very important in the decision to attend a conference. 75% (N = 76) and 37% (N = 37) felt that both content & the speaker, respectively, would most likely cause them to attend a CME activity. The preferences & results do not differ based on years in practice. Unexpectedly web learning is not the preferred method of learning for younger physicians & there is a clear preference for hard copies of materials vs. web-based materials.

**Conclusion:** Despite advancement in educational technology (i.e. web learning, video & tele-conferencing), the majority of respondents still prefer traditional learning formats. CME credits seem to play a significant role in the decision to attend a conference, while the most important factors influencing attendance at CME activities are the content of the program & the speaker responsible for conveying the information.

## 840

#### Gastric Acid Analysis Is a Reliable and Reproducible Measure of Acid Secretion in GERD Patients Treated with Placebo or Pantoprazole

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**Purpose:** To compare the results of 3 separate studies using gastric acid output to assess the consistency of results and the ability of pantoprazole to suppress gastric acid secretion in similar patient populations.

**Methods:** Three different multi-center, randomized, double blind studies enrolled patients with a history of erosive esophagitis and symptoms of GERD who underwent an antisecretory therapy wash out prior to randomization. Although the study designs differed among the three studies, each had an arm that received oral pantoprazole 40 mg tablets for 7–10 days and 2 studies had placebo arms (one with 2 separate placebo arms). Basal acid output (BAO) and maximal acid output (MAO; pentagastrin stimulated, 6.0 µg/kg, sq) were measured at Hour 22–23 and Hour 23–24 after the last dose, respectively, after 7–10 days of therapy. Acid output is the product of  $[H^+]$  × gastric volume for each of four 15-minutes collections, which are added together to provide a one-hour BAO or MAO measurement.

**Results:** In studies with placebo arms the MAOs were  $30.5 \pm 12.8$  (N = 7)<sup>1</sup>;  $29.2 \pm 13.0$  (N = 8)<sup>2</sup>;  $20.9 \pm 14.5$  (N = 24)<sup>2</sup> and the BAOs were  $4.1 \pm 5.2$  (N = 7)<sup>1</sup> and  $3.2 \pm 1.9$  (N = 8)<sup>1</sup>;  $2.8 \pm 3.0$  (N = 23)<sup>2</sup>, respectively. The results of the patients treated with oral pantoprazole 40 mg tablets for 7–10 days are in table below.

**Conclusion:** When performed by experienced operators, gastric acid output measurements are remarkably consistent across different studies in similar patient populations. Acid suppression by pantoprazole is also consistent and reproducible. Gastric acid analysis is a reliable method for quantifying acid secretion and its inhibition. <sup>1</sup> Am J Gastro 2000, 95:626–633 <sup>2</sup> Dig Dis & Sci 2006, 51:1595–1601 (and data on file) <sup>3</sup> Am J Gastro 2006 (Abstract 143), 101(S2): Page S90 (and data on file)

Study	N	MAO mEq/hr (mean ± SD)	BAO mEq/hr (mean ± SD)
A <sup>1</sup>	31	6.5 ± 5.6	0.8 ± 1.3
B <sup>2</sup>	22	6.3 ± 6.6	0.6 ± 0.8
C <sup>2</sup>	52	7.3 ± 4.8	0.6 ± 0.6

## 841

#### Prevalence of Gastroesophageal Reflux Disease as Assessed by the National Ambulatory Medical Care Survey

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**Purpose:** Estimates of the prevalence of GERD have previously used large surveys of the general population. These surveys are unlikely to accurately estimate the prevalence of patients seeking medical care for GERD. This information would be especially useful for future economic estimates of the overall cost of GERD to the US healthcare system.

**Methods:** The U.S. Census Bureau acts as the data collection agent for the NAMCS. Each primary sampling unit consists of physicians randomly assigned to a 1-week reporting period during a calendar year. During this period, a sample of patient visits are recorded using a standardized encounter form. For this study the NAMCS codes for diagnoses and symptoms compatible with GERD were combined into a single categorical variable.

**Results:** From 1995–2004 there were 266,339 ambulatory care encounters for all diagnoses recorded in the NAMCS. Of these, 2,827 (1.1%) were for GERD. Prevalence in both genders was identical. GERD patients were significantly older (53.4 vs. 45.5 years,  $P < 0.001$ ) than non-GERD patients. There was an increase in cases from 1995 (583/100K) to 2004 (1369/100K;  $P < 0.001$ ). This increase was seen in both genders and among whites and blacks. Race was not an independent risk factor for GERD ( $P = 0.51$ ). There was a significant difference in regional rates of GERD (range 883/100,000 in Western U.S. to 1195/100K in Midwest U.S.), however, after adjustment for age, this difference was not significant ( $P = 0.36$ ). GERD was associated with tobacco use (12.6% vs. 9.9% for non-smokers;  $P = 0.028$ ). GERD was not associated with more physician visits per year (3.1 vs. 3.4;  $P = 0.26$ ), and, although statistically significant, office visits for GERD patients averaged only 72 seconds longer (20.5 vs. 19.3 min;  $P < 0.001$ ). Not surprisingly, patients with GERD were far more likely to be prescribed a PPI (OR = 43.7; 95% CI 40.2–47.5,  $P < 0.001$ ).

**Conclusion:** The prevalence of ambulatory care visits for GERD is rising, paralleling the data from other population-based studies. The prevalence is rising for both genders, as well as blacks and whites and is associated with regular tobacco use and increasing age. Frequency and duration of ambulatory care office visits appears unrelated to this diagnosis. Future NAMCS surveys will include BMI data allowing the capability to determine the effects of obesity on trends in GERD-related visits.

## 842

#### Statin Use and the Risk of Cholecystectomy in Women

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**Purpose:** Statins are recently shown to exert beneficial pleiotropic effects beyond reducing serum cholesterol levels. Statins can reduce biliary cholesterol secretion independent of inhibition of cholesterol synthesis, and have been shown to prevent gallstone formation in animals. The effect on gallstone disease in humans is unclear.

**Methods:** We examined the relation of statin use to the risk of cholecystectomy in a large cohort of women. As part of the prospective cohort study on women's health in U.S., the women who had no history of gallstone disease reported biennially if they had undergone cholecystectomy, a surrogate of symptomatic gallstone disease. A validation study was conducted. Based on when the exposures of interest were queried, two follow-up periods were used. In 2000 women were first asked to report separately if they regularly used statins. Statin users were asked to further specify duration of use in two-year categories up to six or more years. Retrospective analysis

for statins using data collected in 2000 to define use from 1994 forward. Prospective analysis for general lipid-lowering drugs was conducted during the same study period. Responses to the 2000 questionnaire indicated that by that year approximately 93% of the cholesterol-lowering drugs used in this cohort were statins. Analysis of statin use included 53,611 women, and analysis of general lipid-lowering drugs use included 56,953 women. Multivariate relative risks were assessed using the Cox model.

**Results:** In the statin analysis we ascertained 2,581 cases of cholecystectomy during 305,197 person-years of follow-up. The multivariate relative risk (R.R.) for current statin users, compared with nonusers, was 0.82 (95% confidence interval (C.I.), 0.70 to 0.96). Among diabetic women, longer duration of statin use ( $\geq 2$  years) was associated with a seventy-five percent risk reduction. Compared with diabetic nonusers, the R.R. for current diabetic users for two or more years was 0.25 (C.I., 0.07 to 0.88). In the general cholesterol-lowering drugs analysis, we ascertained 2,434 cases of cholecystectomy during 298,726 person-years of follow-up. Compared with nonusers, the R.R. for current users of general cholesterol-lowering drugs, mostly statins in this cohort, was 0.86 (C.I., 0.75 to 0.99).

**Conclusion:** Our findings suggest that statin use, particularly among diabetic women, may reduce risk of cholecystectomy.

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#### A Model To Predict Rebleeding Following Endoscopic Therapy for Nonvariceal Upper Gastrointestinal Hemorrhage

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**Purpose:** Following endoscopic therapy, recurrent bleeding occurs in up to 20% of patients with nonvariceal upper gastrointestinal hemorrhage. The objective of this study was to develop a rebleeding score to predict recurrent hemorrhage in these patients.

**Methods:** This was a retrospective cohort study of consecutive patients admitted to a tertiary care hospital between July 1, 1999, and June 30, 2004, with nonvariceal upper gastrointestinal hemorrhage. Patients were evaluated for rebleeding within 30-days of successful therapeutic endoscopy. Two hundred thirty-six patients were identified using the hospital's endoscopic database. Factors for inclusion in the rebleeding score were identified using multivariable logistic regression with stepwise selection. The regression coefficients were converted into integers for score calculation. Internal validation was performed using bootstrapping.

**Results:** Six factors were included in the rebleeding score: Proton pump inhibitor use (-8 points,  $P = 0.056$ ), Endoscopically demonstrated bleeding (5 points,  $P = 0.053$ ), Peptic ulcer (6 points,  $P = 0.018$ ), Treatment with epinephrine monotherapy (7 points,  $p = 0.0026$ ), Intravenous or low molecular weight heparin use (15 points,  $P = 0.0014$ ), and moderate or severe

Cirrhosis (10 points,  $P = 0.032$ ) (PEPTIC). The area under the curve for the score predicting rebleeding was 0.71. Cutoffs were chosen to stratify patients as "low-risk" (score  $\leq -3$ ; 7.6% rebled), "average-risk" (score  $-2$  to  $0$ ; 15.7% rebled), "high-risk" (score  $1$  to  $7$ ; 32.6% rebled), or "very high-risk" (score  $\geq 8$ ; 68.2% rebled).

**Conclusion:** We have developed an easily calculated rebleeding score that predicts recurrent hemorrhage following endoscopic therapy for nonvariceal upper gastrointestinal hemorrhage.[figure1]

844

#### Effects of Lubiprostone, a Chloride Channel Activator, on Cardiac Parameters in Dogs

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**Purpose:** Treatment with lubiprostone, a type-2 chloride channel (CIC-2) activator used for the treatment of adults with chronic constipation, does not result in QTc prolongation in human subjects treated with supratherapeutic doses (up to 144 mcg) (Sprenger *et al*, Gastroenterology 132[4 Suppl 2]:A-325, 2007). Studies were performed to assess cardiac effects of lubiprostone in dogs.

**Methods:** In an *in vitro* assay to evaluate lubiprostone effects on cardiac action potential, isolated canine Purkinje fiber preparations were exposed to increasing doses of lubiprostone (7.5, 75, and 750 pg/mL; 1.5–150 times the highest observed plasma concentration in humans) at 3 stimulus intervals, results of which were compared to time-matched vehicle control sequences. An *in vivo* study evaluated the effects of a single intraduodenally administered (ID) dose of lubiprostone (0, 10, 100, or 1000 mcg/kg) in male dogs. Blood pressure, heart rate, femoral artery blood flow, and electrocardiograms (ECGs) were collected at 7 time points over 2 hours post-dose. A second *in vivo* study evaluated the effects of repeated oral dosing of lubiprostone (up to 50 mcg/kg/day) in male and female dogs over a 39-week treatment period. ECGs were collected prior to dosing and at Weeks 13, 26, and 39.

**Results:** The *in vitro* assay showed no remarkable changes in action potential duration or amplitude, resting membrane potential, or maximum rate of rise of the action potential at any of the concentrations tested. ID administration of lubiprostone had no effect on any cardiac parameter at any dose, with the exception of decreased mean blood pressure (34% maximum) between 10 and 120 minutes post-dose at 1000 mcg/kg, which is 1,250 times the recommended single dose in humans. Over 39 weeks of lubiprostone treatment at doses up to 50 mcg/kg/day ( $>31$  times the recommended daily dose in humans) no abnormal changes in heart rate, QRS duration, QT interval, QTc, PR interval, or R wave were observed in male or female dogs.

**Conclusion:** *In vitro* and *in vivo* testing of lubiprostone in dogs demonstrates a favorable cardiac profile at clinically relevant and supratherapeutic doses. This research was fully funded by Sucampo Pharmaceuticals, Inc.

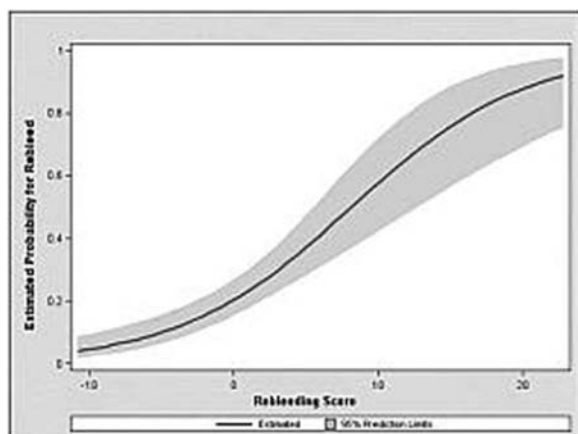
845

#### Antispasmodics Are Safe for Treating Irritable Bowel Patients Age 65 and Older in the Community

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**Purpose:** GI antispasmodics are generally not recommended for patients 65 years and older because of the perception that the elderly are particularly prone to the CNS side effects of these agents and their effectiveness at doses tolerated by this age group is questionable. This has not been our experience, but since HMO's and pharmacies recently have been rejecting or questioning such prescriptions in patients over 64 years, an outcomes study was undertaken to assess this bias against antispasmodics in the elderly.

**Methods:** An outcomes study was set up including all patients (pts) with IBS seen between 1/06–10/06 in our private clinical GI practice in Orlando, FL. Of 545 pts seen with IBS, 104 pts aged 65 and above were encountered, and their characteristics studied from chart review.



**Results:** 85% (88/104) of pts were much better after antispasmodic treatment. 12% (13/104) were somewhat better, and only 3% (3/104) were not any better. Medications used included hyoscyamine, clidinium/chlordiazepoxide, belladonna/phenobarbital and dicyclomine. Dosages were in the usual recommended adult dosage range. Side effects were rare, except for dry mouth (30%) and sleepiness (8%). Interestingly, 87% (90/104) of these pts were considered to suffer with significant stress, anxiety disorder or depression. 23% pts took medications for < 1 year, and 52% of the total population took medications for < 5 years. Of the pts with IBS who were over age 65, their symptoms began before age 35 in 9.6%, age 36–55 in 15.4%, age 56–65 in 27.9% and over age 65 in 47.1%.

**Conclusion:** 1. Antispasmodics and anticholinergics were extremely effective in 85% of pts and somewhat effective in 12%. 2. Antispasmodics were safe when used in this age group and side effects did not limit usage in this cohort, and were essentially those of dry mouth and rarely fatigue. 3. 87% of these pts had significant stress factors, anxiety disorder or depression. 4. Medication usage was usually short lived or intermittent in 75% of pts. 5. IBS symptoms began most commonly over age 65 in this cohort (47%) with 75% of pts developing symptoms over age 55.

## 846

### The Readability of Hepatitis C Health Education Materials

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**Purpose:** Brochures educate patients with hepatitis C virus (HCV) infection about all aspects of their disease. Government regulations require many documents to be written at an eighth-grade level or lower to ensure readability. Data from the National Health and Nutrition Examination Survey suggests that most Americans with HCV infection have an education level of high school or less. Many of these people may lack adequate literacy skills to benefit from such educational tools.

**Aim:** To determine the readability of HCV educational brochures.

**Methods:** Using computer software, Flesch-Kincaid Grade Levels and Flesch Reading Ease scores were measured for selected HCV educational brochures to determine brochure readability. Reading ease scores range from 0 to 100; lower scores indicate increased difficulty in readability.

**Results:** Flesch-Kincaid Grade Levels and Reading Ease scores for brochures were: National Institutes of Health: What I Need to Know About Hepatitis C (6, 68.5), American Liver Foundation (ALF): If you have Hep C (7.3, 65.7), Centers for Disease Control (CDC): Living with Chronic Hep C (7.4, 65.5), CDC: Getting Tested for Hep C (7.4, 65.6), ALF: Coping with HCV Infection (8.9, 54.7), Hepatitis C Connection: Hepatitis C Fact Sheet (9.6, 55), Hepatitis Foundation International: Hepatitis C (11, 45.4), ALF: Hepatitis C (12.5, 36.5), and ALF: Hep C, An Information Source (12.7, 34.4).

**Conclusion:** HCV educational brochures have a wide range of readability scores. Several currently available brochures were rated above the recommended eighth grade reading level. Brochures from government agencies had generally higher readability scores than brochures from other groups and therefore may be more useful to the larger population of HCV patients. Future studies are needed to better characterize the health literacy of patients with HCV infection in order to guide clinicians working with patients with HCV infection.

## 847

### Stress Ulcer Prophylaxis for the Acutely-Ill Patient: What Do Residents Know?

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**Purpose:** Several risk factors for developing stress ulcers (SU) have been identified: mechanical ventilation, head injuries, organ transplant, coagulopathies, and severe burns. In spite of that, unwarranted use of Stress Ulcer Prophylaxis (SUP) is widespread in US hospitals due to the lack of knowledge in this area. Such improper use of medications is costly.

**Methods:** Questionnaires consisting of multiple-choice and short-answer questions were distributed to 125 residents at the Detroit Medical Center, with a response rate of 80% (100). The aims were to gauge residents' understanding of risk factors for developing SU, assess the process in selecting agents, and compare demographic trends. Three forms were excluded from final analysis for being incomplete.

**Results:** Of the 97 respondents, 34% were interns and 66% were more senior residents; 35% were pediatric residents, 42% were internal medicine (IM) residents, 14% were combined pediatrics/IM residents, and 9% were rotating residents from other specialties. Risk factors for developing SU most commonly identified were: high-dose steroid therapy (86% of participants), burns (80%), previous PUD (77%), and recent alcohol/drugs abuse (65%). Established risk factors, such as organ transplant (16%), mechanical ventilation (37%), and head injury (40%), were not as commonly selected. No resident would initiate SUP for patients with coagulopathies. The routine use of SUP for all types of admissions was indicated by 14% of all participants. Receiving high-dose steroids was the most common reason to initiate therapy among pediatric residents (70%), followed by having burns (46%); whereas IM residents chose burns most commonly (57%), followed by high-dose steroids (50%). Proton pump inhibitors were selected as the most effective therapy by 58% of residents, followed by H<sub>2</sub>-Blockers (35%). Diarrhea was the most commonly selected adverse outcome of therapy, followed by pneumonia. Cost of therapy was an interest to only 4% of all respondents.

**Conclusion:** Knowledge on the topic of risk factors for SU, comparison of effectiveness of therapy, and adverse outcomes is lacking among residents. Using steroids by far was the most common reason to initiate therapy, even though it is not an established risk factor in the literature. Most residents did not seem to be aware of some major risk factors. An institution-wide protocol for SUP therapy may need to be in place to minimize the cost of unwarranted therapy and prevent possible adverse outcomes.

## 848

### Patient Phone Calls: Activity-Based Cost Analysis Related to Outpatient GI Practice

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**Purpose:** Phone calls to a physician's office from patients occupies the time of many personnel in a gastroenterology practice. The objective of this study was to evaluate the time impact and cost effect of these phone calls on an out-patient GI practice with focus on medication related questions.

**Methods:** Prospective blinded study involved 100 consecutive calls that were passed to the nursing staff by the receptionist. Nurses were blinded as to the intent of the study and were told it was a quality assurance program. Time logs were assessed for each stage of the consecutive calls including the receptionist, nurse and physician stages. Standard office policy was that the physician review all telephone call communications.

**Results:** Call times for medication related calls were analyzed with time rounded to the nearest min. 30% of calls were medication related. Of these, 10% were due to side effects of medication prescribed, 50% due to lack of efficacy, 5% due to questions concerning medication dose, 20% related to cost and availability, and 15% for other reasons. Medication categories for the calls were IBD: 26%, hepatic: 22%, acid/peptic: 21%, IBS: 20%, and other: 11%.

Please refer to Table 1.

The average cost incurred to the practice by a medication related call was \$20.29. Other additive potential costs such as overtime or other "opportunity costs" were not assessed by this analysis.

**Conclusion:** Using an activity based cost accounting analysis, these data show that medication related patient calls to physician offices have considerable indirect related costs that are expenses incurred by the physician practice. Studies are underway, using similar survey data to compare these results to the impact of electronic medical records.

**Table 1.** Average Time per Call

Personnel	Mean Time (min)	Time Range (min)	Payscale (\$/Hr)
Receptionist	1	1–3	15
File Clerk	3	2–5	12
Nurse	10	3–25	26
Physician	3	1–15	300
Transcription*	2	1–4	17

\*(20% of Calls)

## 849

### Patient Underreported Use of NSAIDs in GI Practice: A Prospective Office-Based Survey

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**Purpose:** Non-steroidal anti-inflammatory drugs (NSAIDs) are one of the most commonly used classes of medications worldwide. It is estimated that more than 30 million people take NSAIDs daily. We examined the underreported use of NSAIDs on a preliminary office intake assessment questionnaire of patient reported medications.

**Methods:** A prospective questionnaire was administered to patients following written and verbal confirmed report of "current medications" to nursing staff. 100 patient surveys performed for consecutive patients seen in a private GI practice. After patients listed their "current medications", they were given a survey and asked to acknowledge any use of 30 non-prescription formulations that contained NSAIDs. Patients filled these surveys while waiting for M.D. The educational level of all participants was assessed.

**Results:** Of the 100 surveys completed, 6% of patients had not completed high school, 19% had completed high school, 8% had started but not finished college, 54% had completed college, 2% had started but not finished graduate school, and 11% had completed graduate school. The educational level of the patients did not correlate with underreporting of NSAID usage. On the survey, 18% of patients noted use of an NSAID listed that had not been reported verbally to nursing staff. 8% of those patients reported daily use, 15% weekly use and 76% reported use within the last month. Patients were then asked in the questionnaire as to the reason for not reporting medication intake to nurse. 14% stated they were never asked about the specific medication, 22% did not think the medications were important enough to list, 34% bought the medication with prescriptions, and 30% noted their reason as their doctor did not prescribe the medication to them.

**Conclusion:** Using a prospective questionnaire in a private practice GI office, these data show that patients underreport use of non-prescription NSAIDs. Based on the data, it is clear that this underreporting can have a detrimental effect on procedure related as well as long-term patient care. Future studies would be needed to examine the incidence of side effects due to underreporting of NSAIDs.

## 850

### Derivation and Validation of an Algorithm To Identify Helicobacter pylori Infected Patients Using Administrative Data

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of Care and Utilization Studies; Micheal E. DeBakey VAMC, Houston, TX and Department of Medicine, Baylor College of Medicine, Houston, TX.

**Purpose:** To validate VA administrative data for the diagnosis of *H. pylori* infected patients.

**Methods:** National pharmacy, inpatient and outpatient administrative databases identified patients with an ICD-9 code for *H. pylori* (041.86) and those with prescriptions for eradication therapy from 01/01/03 to 12/31/03. Primary chart abstraction was used to confirm diagnosis of *H. pylori* based on antibody serology, urease breath testing, histopathology, or progress notes. Multivariable regression assessed predictors of *H. pylori* infection considering: prescription of eradication drug therapy, ICD-9 code, EGD procedure code, source of diagnostic code (inpatient or outpatient), age, gender and race. The c-statistic was calculated to assess the discriminant ability of the algorithm. Once derived this algorithm was validated in a cohort of patients from calendar year 2005 (N = 312).

**Results:** The test cohort consisted of 581 patients (378 potential cases; 203 random controls) who were primarily male (94%), Caucasian (59%) and elderly (67 years [SD 10]). ICD-9 code 041.86 had the greatest positive predictive value (PPV) for *H. pylori* (PPV 100% if from an inpatient encounter; PPV 97.4% if from an outpatient encounter). Evidence of eradication drug therapy was associated with a PPV of 73.7% (triple therapy) and 97.7% (quadruple therapy). Multivariable regression revealed the strongest predictors to be outpatient ICD-9 code 041.86 (OR 8.1; 95% CI: 7.0–9.1); eradication drug therapy (OR 7.4; 95% CI: 6.6–8.3); EGD (OR 3.5; 95% CI: 3.3–3.6); and age  $\geq 70$  (OR 1.2; 95% CI: 1.1–1.4). A diagnostic algorithm including eradication drug therapy, ICD-9 diagnostic code 041.86 and age  $\geq 70$  yielded a c-statistic of 0.93, suggesting excellent discriminant ability. When this algorithm was tested in a validation cohort from calendar year 2005, the PPV was 97.9% with a NPV of 98.8%.

**Conclusion:** Administrative data can be used to accurately diagnose *H. pylori* infected patients. The optimal diagnostic algorithm includes presence of eradication drug therapy overlapping with an outpatient ICD-9 code 041.86 among elderly adults.

## 851

### Cost-Benefit of PPI Gastroprotection among Elderly NSAID Users

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**Purpose:** Our aim was to quantify national cost-benefit of proton pump inhibitor (PPI) gastroprotection in a cohort of elderly NSAID users.

**Methods:** Veterans  $\geq 65$  years prescribed an NSAID or coxib at a VA facility (01/01/00–12/31/02) were identified from national prescription fill data and records linked to VA and Medicare inpatient, outpatient and death files. Using our published algorithm, we defined UGIE and assessed related endoscopic, radiological or surgical procedures, ambulatory visits and inpatient hospitalization days. The VA National Average Cost Dataset was used to assess healthcare utilization costs, apportioned as recommended by published methodology. Pharmacy costs, from the VA Pharmacy Benefits Management program, were considered cumulative from the index NSAID prescription to the UGIE. Each person-day of follow-up was assessed for exposure to NSAID, coxib and overlapping PPI. Regression models assessed whether PPI gastroprotection resulted in reduced healthcare use, while adjusting for demographics; UGIE risk factors; co-morbidity; prescription channeling (i.e., propensity score); geographic location and multiple time-dependent pharmacological covariates, including aspirin, anticoagulants, antiplatelets and statins.

**Results:** In 481,495 veterans, 3,205 UGIE (97.3% male; 78.6% white; mean age, 73.9 [SD 5.7]), occurred in 293,594 person-years of follow-up. Of these UGIE, 36.9% were treated by the VA (i.e., VA-UGIE), costing \$5.05 million, 97% of which (\$4.9 million) was related to medical resource use and \$150,000 to pharmacy costs. Of VA-UGIE patients, 50% were hospitalized;

the 33.8% prescribed a PPI were less likely to be hospitalized (OR 0.39; 95% CI: 0.30–0.52) and had a lower median total medical cost than those not prescribed a PPI (\$522.14 [IQR 1935] vs. \$1,268.91 [IQR 4176];  $P < 0.001$ ). PPI prophylaxis for an NSAID-related UGIE requires an additional \$234 per veteran. However, this increase is offset by a \$2,019 reduction in total medical costs per veteran.

**Conclusion:** PPI gastroprotection for high-risk elderly patients is associated with fewer NSAID-related UGIE and reduced hospitalization and associated resource costs. Reduced resource costs offset higher pharmacy-related costs, making PPI gastroprotection beneficial for elderly veterans.

## 852

### Healthcare Costs and Clinical Sequelae Associated with Constipation in a Managed Care Population

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**Purpose:** In addition to a high cost burden, patients with constipation are likely to suffer from a high incidence of gastrointestinal (GI)-related clinical sequelae. We examine changes in health care costs and sequelae in patients with constipation before and after initial diagnosis compared to matched controls.

**Methods:** The i3 Innovus LabRx database was retrospectively analyzed. Patients diagnosed with constipation (ICD-9 564.0×) between 1/1/03 and 12/31/05 were identified ( $N = 48,585$ ) and demographically matched in a 1:2 ratio with controls ( $N = 97,170$ ). An index date for the constipation group was defined as the date 3 months prior to the first observed constipation diagnosis. For controls, the index date corresponded to that of their respective match in the constipation group. Per patient charges for medical services and prescriptions, and rates of GI-related sequelae were assessed over 12 months prior to and following the index date.

**Results:** Total health care charges per patient with constipation were \$9,305 pre-index compared to \$17,799 in the post-index period (+\$8,494;  $P < 0.0001$ ). Total charges for controls were \$5,967 pre-index and \$7,151 post-index (+\$1,183;  $P < 0.0001$ ). After controlling for comorbidities, prevalence of cancer, opioid use, and Charlson Score between the pre- and post-index periods via linear regression, total charges per patient with constipation remained substantially higher (+\$3,664;  $P < 0.0001$ ) post-index vs. pre-index. Charges for controls remained \$701 higher post-index ( $P < 0.0001$ ). Logistic regression showed that patients with constipation had a substantially and significantly ( $P < 0.0001$ ) greater likelihood of intestinal impaction (odds ratio [OR] = 6.6), anal fissures (OR = 5.0), hemorrhoids (OR = 4.2), volvulus (OR = 10.3), intestinal obstruction (OR = 4.1), and rectal ulcers (OR = 4.8) during the post-index period compared to pre-index. Overall, patients with constipation were 4.5 times more likely to have any clinical sequelae post-index (OR = 4.5;  $P < 0.0001$ ), while no significant change was found among controls.

**Conclusion:** Persons with constipation have greater health care costs and GI-related sequelae post-index period compared to pre-index. Demographically similar patients without constipation have a lower prevalence of these sequelae with no pre- to post-index change. Increased prevalence of these sequelae may contribute to the total cost burden of constipation. Current standards of care may not be sufficient to reduce this burden.

## 853

### Outcomes of Recurrent Abdominal Pain (RAP) in Children and Responses to a Multidimensional Measure for RAP (MM-RAP): A Follow-Up Study

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**Purpose:** Recurrent abdominal pain (RAP) is a common problem in children and adolescents. The aims are: 1) to characterize the course of children with RAP, 2) to evaluate the diagnostic outcomes of RAP, 3) to compare responses of a newly developed measure for RAP across the different diagnostic categories of RAP.

**Methods:** We conducted a prospective 2 year study of children diagnosed with RAP during their first visit to the Pediatric Gastroenterology Clinic at Texas Children's Hospital and who were followed-up. At their initial visit, the eligible child/parent completed a multi-dimensional measure for RAP (MM-RAP) consisting of 4 scales (pain intensity scale, symptoms scale, disability scale, and satisfaction scale). The final diagnosis was defined as the diagnosis at their last visit. Outcomes were classified into 3 categories: functional RAP, organic RAP, and Gastroesophageal Reflux Disease (GERD). The responses of the MM-RAP were analyzed by One-Way ANOVA analysis among the 3 RAP outcome groups.

**Results:** One hundred and forty one children ages 4 to 18 years (44% boys) participated. The mean follow-up period was 50 weeks. The final diagnoses were functional RAP in 46%, organic RAP in 24%, and GERD in 30%. Neither age nor sex predicted the outcome. The total scores for the pain intensity scale were significantly higher among children with functional RAP than organic RAP or GERD (19.7 ( $\pm 3.5$ ) vs. 14.2 ( $\pm 4.7$ ) and 13.1 ( $\pm 4.2$ ); respectively,  $P = .001$ ). Although the non-pain symptoms total score did not differ between the three outcome groups, independent items within the scale, i.e. diarrhea, vomiting, and heartburn were significantly higher among children with organic RAP and GERD compared to functional RAP. The scores for pain disability and health satisfaction scales were similar among the three outcome groups.

**Conclusion:** The MM-RAP discriminated between functional and organic RAP across the studied population. Children with functional RAP report more intense pain than children with organic RAP or GERD. Neither the disability scale nor the satisfaction scale differentiated between the functional and organic RAP.

## 854

### Sequential Therapy Is Superior to Standard Therapy for Treatment of *Helicobacter pylori* Infection: A Systematic Review and Meta-Analysis

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**Purpose:** Authorities continue to recommend standard PPI-based triple or quadruple therapy for the treatment of *H. pylori* infection despite failure of eradication in around a quarter of patients. Sequential therapy (ST) (5 days of PPI + 1 antibiotic followed by 5 days of PPI + 2 other antibiotics) may be more efficacious.

**Methods:** We performed a systematic search for randomized controlled trials (RCTs) comparing ST with standard therapy for *H. pylori* infection in Medline, EMBASE, and the Cochrane Central Register of Controlled Trials using Pubmed, Google Scholar and Ovid as search engines without language restriction. We also hand searched the references of original/review articles and evaluated symposia proceedings, poster presentations and abstracts from major gastrointestinal meetings. Relative risks (RR) were calculated for individual trials; data were pooled using a fixed effects model. Relative risk reduction (RRR), absolute risk reduction (ARR) and number needed to treat (NNT) were calculated and are reported with 95% confidence intervals (CI). Study quality was assessed with the Jadad scale. Results were subjected to sensitivity analysis.

**Results:** 8 RCTs comprising 2202 patients (1071 men) met eligibility criteria. Mean age ranged from 9.9–70 years. 1095 patients were randomized to sequential therapy and 1107 to standard therapy. ST was superior with respect to eradication rates; RRR = 22% (95% CI: 18–27%), ARR = 17% (14–20%), NNT = 6 (5–7), and for ulcer healing; RRR = 17% (10–25%), ARR = 11% (7–16%), NNT = 9 (6–14). Compliance was similar in both arms (RR 0.99, 95% CI: 0.97–1.01). ST was superior in adults (RRR = 22% (18–27%), ARR = 17% (14–20%), NNT = 6 (5–7)), as well as in smokers



(RRR = 25% (9–43%), ARR = 19% (9–29%), NNT = 5 (3–11)); and in patients with non-ulcer dyspepsia (NUD) (RRR = 25% (18–33%), ARR = 19% (14–23%), NNT = 5 (4–7)). When evaluating only RCTs of high quality (Jadad score  $\geq 3$ ) there was still a benefit to ST (RRR = 17% (11–24%), ARR = 14% (9–18%), NNT = 7 (5–11)). Lack of significant heterogeneity was noted among RCTs, except for ulcer healing. Side effect profile was similar in both arms.

**Conclusion:** ST appears superior to standard therapy for eradication of *H. pylori* infection and ulcer healing. It also produced superior eradication rates in smokers and in patients with NUD. These outcomes were consistent by sensitivity analysis. However, all identified RCTs were from Italy, and results may not be replicable in the US. This approach should be tested in US-based RCTs.

855

### GI Endoscopy Nurse Experience Predicts Polyp Detection during Screening Colonoscopy

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**Purpose:** While factors that predict polyp detection during screening colonoscopy have been described, the effect of GI endoscopy nursing experience level on polyp detection is unknown. The aim of this study was to determine whether nurse experience is associated with rates of polyp detection.

**Methods:** We performed a retrospective analysis of screening colonoscopies at the University of North Carolina Hospitals between August 2003 and 2005. Procedures were limited to those performed by attendings without trainee involvement. Nurse experience was measured in weeks from the initial start date to the procedure date for each endoscopy nurse. The primary outcome was the detection of any polyp. The secondary outcome was the detection of multiple polyps. Additional variables related to both the procedure (bowel preparation quality, cecal intubation rate, withdrawal time) and the patients (age, gender, ASA score, BMI, comorbidities, and past surgical history) were extracted from our electronic endoscopy database. Descriptive statistics, bivariate analysis, and multivariable logistic regression were performed. The study was approved by the Institutional Review Board of UNC.

**Results:** Any polyp was detected in 44% of the eligible 3,631 screening colonoscopies. Multiple polyps were detected in 23%. Twenty-nine nurses were employed in our endoscopy unit during the study period, 19 of whom were new to gastroenterological nursing. Increased polyp detection was associated with increased withdrawal time, reaching the cecum, increased patient age, increased patient BMI, and better quality bowel preparation. For nurses with 6 months of experience or less, any polyp was detected in 40.3% of procedures compared with 46.0% of procedures for nurses with more than 6 months of experience (OR 1.3, 95% CI: 1.1–1.5,  $P = 0.002$ ). Similarly, for nurses with 6 months of experience or less, multiple polyps were detected in 18.2% of procedures compared with 25.5% of procedures for nurses with more than 6 months of experience (OR 1.5, 95% CI: 1.3–1.8,  $P < 0.001$ ). These relationships held after adjusting for potential confounding patient and procedure variables.

**Conclusion:** Nursing experience of six months or less is associated with lower rates of polyp detection, independent of physician withdrawal time, bowel preparation, cecal intubation rate, and other factors that might influence detection. These findings may have implications for nurse training as well as quality of colorectal cancer screening programs that utilize colonoscopy.

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### Persistence with Infliximab Therapy Reduces Crohn's Disease Related Medical Costs

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**Purpose:** To evaluate the impact of persistence with infliximab treatment on medical costs among patients with Crohn's disease (CD), utilizing a managed care database.

**Methods:** A retrospective study using PharMetrics managed care plan database in the United States from July 1, 1999 through June 30, 2005, was conducted. Patients newly initiated on infliximab, continuously enrolled for 12 months before and after their index infliximab claim, and having at least 2 diagnoses of CD, one of which occurred in the pre-index period were included. Persistence (%) was defined as the number of days between the first infliximab claim and the last infliximab encounter, divided by 365 and multiplied by 100. Two mutually exclusive cohorts were defined based on their levels of infliximab persistence: patients who were persistent greater or equal to 80%, and those who were persistent less than 80%. CD-related medical costs (those in which CD was the diagnosis on the claim) in the 12-month post-index period were computed for each patient. The cost of adverse events could not be identified separately in this analysis. Univariate differences between the persistent and non-persistent cohorts were assessed using Mann-Whitney and chi-square tests.

**Results:** 480 patients were included, 251 (52.29%) with a persistency ratio  $\geq 80\%$  and 229 (47.71%) with a persistency ratio  $< 80\%$ . 55% were female and the mean age was 36.9 years. The  $\geq 80\%$  persistency cohort had lower CD-related medical costs compared with the  $< 80\%$  persistency cohort (\$4,380.21 vs \$8,570.11; ns), primarily driven by inpatient costs (\$2,014.31 vs \$5,981.51;  $P < 0.001$ ). Costs were also higher for emergency room and outpatient levels of care in the lower persistency cohort.

**Conclusion:** This study indicates that a higher persistence rate with infliximab therapy is associated with lower CD-related medical costs, primarily driven by decreased inpatient hospital costs. Future studies to examine the impact of persistence with infliximab on clinical and humanistic outcomes are recommended.

857

### Increased Inpatient Utilization Following Colectomy in Ulcerative Colitis in the Medicare Population

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**Purpose:** To examine inpatient hospital utilization following colectomy in pts covered by Medicare who have ulcerative colitis (UC).

**Methods:** A retrospective analysis was conducted using claims from the Medicare Standard Analytic Files 5% sample database between Jan 1, 2001 and Dec 31, 2005. Pts were identified as having UC using diagnostic codes (ICD-9 codes 556.x) and were limited to those who had a procedure code indicating colectomy (45.7x), and a diagnosis of UC prior to that date. Pts with a subsequent diagnosis of Crohn's disease were eliminated from this analysis. The first procedure was chosen if the beneficiary had multiple 45.7x procedures (these are partial excisions, so a beneficiary could have multiple procedures over time). The study design consisted of a 12-mo pre-colectomy period and 12-mo post-colectomy period. Medicare participation was required for the year prior to the colectomy, and the pt had to be alive during the 12-mo post-colectomy period. Inpatient hospital costs and resource utilization were evaluated 12 mos before and 12 mos after the quarter in which the colectomy occurred. All costs are presented in 2005 US dollars.

**Results:** A total of 905 pts with UC who had a claim for colectomy were included in the analysis. Total inpatient costs (\$19,778 vs \$23,765) and average length of stay (ALOS) (15.2 days vs 18.3 days) increased following colectomy, while mean number of admissions did not increase significantly.

**Conclusion:** Inpatient hospital utilization and subsequent costs increased during the 12-mo period following colectomy in the Medicare population. Although the mean number of admissions was similar, length of stay and costs were higher. Additional analyses along with larger samples are needed

to determine the extent of these services and reasons for increased inpatient utilization.

Mean Inpatient Cost and Utilization Pre- and Post-Colectomy

	Pre-colectomy	Post-colectomy	P-Value
Total Inpatient (N = 222)			
Costs (\$)	\$19,778	\$23,765	0.0001*
Mean number of admissions	2.2	2.3	0.0534
ALOS	15.2	18.3	0.0011*

\* $P < 0.05$ ; paired t-test

## 858

### Collagenous and Lymphocytic Colitis in Celiac Disease: Evaluation of Standardized Morbidity Ratios

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**Purpose:** Celiac disease (CD) and microscopic colitis (MC) occur together in some patients, however the actual prevalence of MC in CD is not known. Using a large data base of patients with CD seen in a university based center we investigated if the occurrence of MC and its subtypes: lymphocytic colitis (LC) and collagenous colitis (CC) is higher in CD than in the general population, via analysis of standardized morbidity ratios (SMR).

**Methods:** Our prospectively maintained database of 1009 patients (seen between 1981 and 2006) with CD at the Celiac Disease Center of Columbia University was analyzed. We calculated SMRs for overall MC, LC, CC and gender-specific MC, LC and CC by using the epidemiological study in general population conducted in Minnesota between 1985 and 2001 as the reference group.

**Results:** Forty-four patients (4.3%) with MC were identified (CC: 11 [1.1%] and LC: 33 [3.2%]). Mean age of diagnosis of CD in those without MC was significantly younger than those with MC ( $42.7 \pm 17.9$  vs  $53.2 \pm 14.7$ ,  $P < 0.0001$ ). There was no difference in the gender distribution in the MC group compared to the whole CD cohort (female:male: 2.1/1 for CD vs 3.9/1 for MC,  $P = 0.13$ ). However, among the two subtypes of MC, CC showed a striking female predominance (female: male ratio-2.7:1 for LC and 11:0 for CC,  $P = 0.05$ ). Based on the data from an epidemiological study of MC in the general population conducted in Minnesota, the SMR was 72.39 (95% CI: 52.52–95.36) for MC; 46.70 (95% CI: 23.05–78.13) for CC and 88.65 (95% CI: 60.87–121.32) for LC. Among females, the SMR was 72.25 (95% CI: 50.30–98.17) for MC, 51.57 (95% CI: 25.45–86.28) for CC and 88.53 (95% CI: 56.66–127.50) for LC; while among males the SMR was 72.93 (95% CI: 33.06–128.36) for MC; 0 for CC and 88.98 (95% CI: 40.34–156.60) for LC, respectively. Of 44 MC patients, 63.6% were diagnosed after CD, because of persistent diarrhea despite a gluten-free diet while 25% were diagnosed simultaneously with CD and 11.4% diagnosed prior to CD.

**Conclusion:** Our study demonstrated that MC is more prevalent in CD than in the general population and occurs in those diagnosed with CD when they are older. LC has a stronger association with celiac disease than CC. CC occurs only in females with CD, while LC occurs in both genders. MC should be suspected in CD when there is a poor response to a strict gluten-free diet.

## 859

### Patients That Do Not Speak English Miss Fewer Clinic Appointments Than English Speaking Patients

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**Purpose:** Prior studies of healthcare outcomes reveal inequities among vulnerable populations; however, it has not yet been established whether deficits in access or utilization are the source of disparity. This study aimed to determine whether non-English speakers and minority patients with established care access exhibit lower rates of utilization of gastroenterology care than English speakers and white patients.

**Methods:** Case-control study performed in a diverse urban population served by an established safety net health system. Subjects included all patients referred and scheduled for a gastroenterology clinic appointment between 05/2005 and 08/2006. The primary outcome was whether a subject showed for their clinic appointment. Predictor variables included age, gender, race/ethnicity, language, socioeconomic measures, appointment wait time, substance abuse and psychiatric history, and primary clinic type. Multivariable logistic regression and classification tree analysis were used to analyze the data.

**Results:** 1,833 subjects were included (683 no-shows and 1,150 shows). In a multivariable analysis, subjects speaking primarily Spanish or an Asian language were more likely to show for a clinic appointment (odds ratio for missing the appointment = 0.42 and 0.56, respectively,  $P < 0.001$ ), than English speakers (see table). Results for race/ethnicity were mixed. In the classification analysis, language was the variable most predictive of utilization.

**Conclusion:** Surprisingly, among patients with established care access, not speaking English was associated with improved rates of gastroenterology care utilization. This unexpected association suggests that language may be a surrogate marker for mechanisms underlying these findings, such as cultural identity, patient-provider communication, or immigration status. Further study is indicated to uncover the role of such mechanisms in vulnerable populations.

Logistic regression of factors associated with not showing for a clinic appointment

Independent Variables	Adjusted Odds Ratio (95% CI)	P Value
Language*		<0.001
–Spanish	0.42 (0.28, 0.63)	
–Asian language	0.56 (0.38, 0.82)	
Ethnicity†		0.001
–Black	1.55 (1.15, 2.08)	
–Hispanic	1.53 (1.06, 2.22)	
–Asian	0.95 (0.66, 1.38)	

Odds ratios represent odds of not showing for a clinic appointment. \*Languages are compared with English. †Race/ethnicity is compared with white.

## 860

### Esophageal Adenocarcinoma and Barrett Esophagus Registry Consortium

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**Purpose:** Progression from Barrett esophagus (BE), a premalignant epithelium, to esophageal adenocarcinoma (AC) likely involves the accumulation of genetic events that impact signals important for cell proliferation, survival, angiogenesis, immune escape, and invasion. Identification and validation of markers requires the resources of a large bank of serially collected, well-characterized fresh-frozen and formalin-fixed tissue, blood, demographic, symptom and risk factor data.

**Aims:** Resource created to facilitate the identification of: 1) genetic pathways important in the neoplastic transformation from BE to AC; 2) novel

biomarkers of risk, early detection, response to treatment; and 3) novel therapeutic or chemoprevention targets.

**Methods:** Since 2001, at Mayo Clinic Rochester (MCR), and 2005, at Mayo Clinic Jacksonville (MCJ), participants provide demographic/clinical information and complete baseline/annual questionnaires. Blood collected once; tissue collected at every clinically indicated endoscopy/surgery. Mayo Clinic Arizona is in the process of joining this effort.

**Results:** As of June 2007, at MCR, 2838 unique patients have met entry criteria of which 1602 (56%) have been enrolled, 651 (23%) declined, and 426 are being processed. Enrolled patients include: 841 BE alone, 291 BE with AC, 189 AC alone, 108 squamous cell carcinoma (SCC) patients (controls), 3 patients with AC and SCC, 4 patients with BE, AC and SCC features, and 157 AC of the gastroesophageal junction. Blood and tissue have been collected at least once from 1380 and 673 unique participants, respectively. At MCJ, 55 of 85 (65%) patients have been enrolled.

**Conclusion:** The Esophageal Adenocarcinoma and Barrett Esophagus (EABE) Registry Consortium is a multi-center multi-disciplinary Academia-NIH-Industry collaborative effort designed to prospectively enroll consecutive patients with Barrett esophagus and esophagus cancer, to collect fresh-frozen/formalin-fixed tissue, blood, demographic, symptom and risk factor data to facilitate bench-to-bedside translational discoveries.

## 861

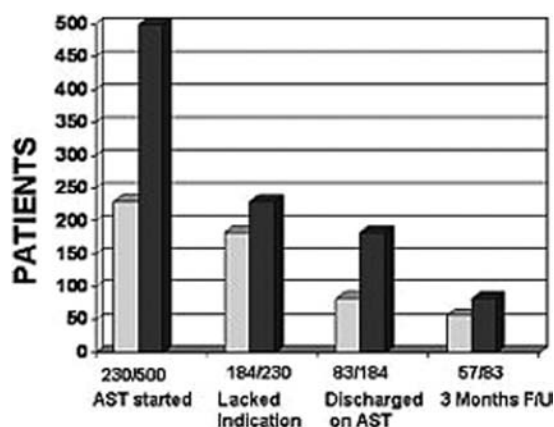
### Use of Acid Suppression Therapy in Hospitalized Patients – Going beyond the Indications

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**Purpose:** Acid suppression medications are among the top 5 medications prescribed in hospitalized patients. There are unequivocal indications outlined for their usage by FDA. We postulate that many patients are inappropriately started and discharged on acid suppression therapy (AST). The aims of our study is to determine the frequency and validity of such prescriptions on General Medicine wards.

**Methods:** Chart review of 500 patients admitted consecutively to a University Hospital was done. Patients who received at least a dose of AST were included. Patients who spent any time in ICU or who were on AST on admission were excluded. Accepted indications were as outlined by the FDA. Categorical variables like demographics, admitting diagnosis, comorbidities, LOS were analyzed with 'starting the patient on acid suppression therapy' and 'discharge on acid suppression' as outcome variables. Those discharged on AST were followed up at 3 months.

**Results:** 230/500 (46%) patients were started on AST on admission. 184/230 (80%) of the patients lacked an indication for initiation of AST. No known cause documented (39%) followed by stress ulcer prophylaxis in low risk patients (23%) were top 2 reasons for inappropriate usage. Most common



reasons for admission were infectious disease (26%) and gastroenterology (15%) related diagnosis. 83/184 (45%) of patients were discharged on inappropriate AST. No significant difference in categorical variables in patients who were discharged on unnecessary AST vs. in whom it was discontinued. On 3 months follow up 68% of these patients were still on inappropriate AST.

**Conclusion:** Our study reveals that not only AST is over prescribed in hospitalized patients but a significant number of patients are also discharged on it without a valid indication. Given the cost and recent data associating AST with complications, its prescription needs to be critically questioned. Educating house staff, strict guidelines for starting AST and emphasizing the importance of medication reconciliation are some of the simple interventions that can help prevent unnecessary prescription of AST.[figure 1]

## 862

### The Direct and Indirect Cost Burden of Crohn's Disease

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**Purpose:** To estimate the direct medical costs and indirect costs (productivity related) for commercially-insured patients with Crohn's Disease.

**Methods:** Data were obtained from the 1999 to 2005 MarketScan Commercial Claims and Encounters (CCA), Medicare Supplemental, and Health and Productivity Management databases. Patients with a diagnosis of Crohn's Disease and at least a 1-year disease-free pre-period were found resulting in 6,569 nonelderly patients with Crohn's Disease and 1,628 elderly patients with Crohn's Disease.

12-month direct medical care expenditures (medical and prescription drug) for patients with Crohn's Disease were compared to expenditures among an equal number of propensity-score matched comparison group members. Propensity scores were estimated via demographic characteristics and comorbidities. Indirect costs, as measured by absenteeism and short-term disability costs, were compared for a sub-sample of employees in each group. Regression analysis controlled for demographic and case mix factors. A range of cost burden estimates were produced by varying the estimation and matching techniques.

**Results:** Average 12-month direct medical care expenditures were \$5,299 for nonelderly and \$8,348 for elderly comparison group members. Average estimated direct medical expenditures for patients with Crohn's Disease exceeded comparison group members by as much as \$16,388 for nonelderly patients and \$8,648 for elderly patients (all  $P < .01$ ).

Absenteeism costs were \$5,097 for employees with Crohn's Disease, although this was not significantly different from the comparison group. Short term disability expenditures were about \$1,700, which was double the amount for the comparison group ( $P < .05$ ).

**Conclusion:** Crohn's Disease is a very costly disorder and merits consideration as interventions are developed to manage the burden of disease and improve productivity.

## 863

### Increased Healthcare Utilization Following Colectomy in Ulcerative Colitis

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**Purpose:** To examine healthcare resource utilization in patients with ulcerative colitis (UC) following colectomy.

**Methods:** A retrospective analysis was conducted using medical and pharmacy claims from the PharMetrics database between January 1, 2000 and June 30, 2005. Patients were required to have 2 distinct claims for UC (ICD-9 codes 556.x) and were limited to those who had a CPT code indicating colectomy (44140–44160), and a diagnosis of UC prior to that date. The study design consisted of a 12-month pre-colectomy period and 12-month post-colectomy period. Continuous enrollment was required for the entire two-year period. Healthcare resource utilization was evaluated 12 months before and 12 months after the colectomy date. The outcomes of interest included healthcare encounters for the following levels of care: inpatient, outpatient, emergency room, physician, laboratory, and drug costs. Basic population characteristics were also examined, including demographics and overall patient comorbidity burden (Charlson Comorbidity Index).

**Results:** A total of 411 patients with UC who had a claim for colectomy were included in the analysis. Over half of the patients were male (51.7%) and the mean age was 46 years. The mean Charlson Comorbidity Index score was 4.4. Total utilization of services increased following colectomy, including inpatient encounters and outpatient encounters, all at significant levels ( $P < 0.05$ ).

Mean Resource Cost and Utilization Pre- and Post-Colectomy

	Pre-colectomy	Post-colectomy	P-Value
Total Healthcare Visits	26.6 (19.3)	39.4 (33.6)	<0.0001
Inpatient encounters	0.9 (1.1)	1.8 (1.7)	<0.001
Outpatient visits	8.7 (10.9)	19.4 (24.9)	<0.001
Emergency Room visits	0.8 (1.4)	0.9 (1.6)	0.2583
Physician visits	13.9 (11.7)	14.9 (13.9)	0.1595
Laboratory visits	2.1 (3.3)	2.2 (4.3)	0.7790

**Conclusion:** Healthcare utilization increased during the 12-month period following colectomy, driven by increases in inpatient and outpatient visits. Additional analyses are needed to determine the extent of these services and reasons for increased service utilization.

## 864

### Maintenance Therapy with Infliximab Reduces Hospitalization and Surgery in Crohn's Disease

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**Purpose:** To assess the impact of maintenance versus episodic infliximab therapy on hospitalizations and surgery in patients with Crohn's disease (CD).

**Methods:** A retrospective analysis of claims data was conducted from the Marketscan Commercial Claims and Encounters database from 2000 to 2003 for claimants with CD (ICD-9 codes, 555.0, 555.1, 555.2 or 555.9) who had an induction regimen (3 infusions) of infliximab in 2003. Continuous enrollment for 12-months pre and 12-months post the index infusion date in 2003 was required. Patients were excluded if they had infliximab infusions in 2001 or 2002. Cohort analyses were conducted for three distinct cohorts: 1) 1–2 infliximab infusions; 2) 3–4 infliximab infusions; 3) 5 or more infliximab infusions.

**Results:** Analyses were conducted on 126 patients who met the inclusion criteria. The majority of patients were female (53.2%) and the mean age was 49.5 years. Among the cohort with 5 or more infliximab infusions ( $N = 34$ ), 20.6% required hospitalization, as compared to 37.5% of the cohort with 1–2 infusions ( $N = 48$ ) and 34.1% of the cohort with 3–4 infusions ( $N = 44$ ). The cohort with 5 or more infliximab infusions also had fewer mean hospitalizations (1.29 vs. 1.83 and 1.47, ns), and shorter lengths of stay (5.11 days vs. 5.64 days and 5.91 days, ns). In addition, the percentage of patients

requiring surgery was decreased for the 5 or more infusion cohort (24%) as compared with the other cohorts (40% each).

**Conclusion:** Although non-significant, the results of this analysis indicate that when treating CD with a maintenance schedule of infliximab, the number and length of hospitalizations are reduced, and the percentage of patients requiring surgery decreases. Infliximab should be used on a maintenance schedule rather than episodically (ie: treat flares) in order to optimize treatment outcomes.

## 865

### Patient Reported Quality of Life Following Surgery in Ulcerative Colitis

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**Purpose:** To assess the impact of surgery on quality of life (QOL) in ulcerative colitis (UC).

**Methods:** A random digit dial phone survey of 1,000 pts with UC in the US was conducted. Respondents were selected from an opt-in database of 17 million US consumers, of which 40,000 self-identified as having UC. Of the 40,000 potential respondents, about 19,000 had confirmable contact information, and were used as targets to arrive at the desired sample of 1,000. Contact was attempted with 7,900 potential respondents, and the overall response rate was 13% (1000/7900). The survey consisted of an interview lasting about 27 minutes. Information was gathered regarding prior surgeries for UC, including total colectomy and various QOL indicators. Summary statistics were calculated.

**Results:** Of the 1,000 respondents, 19.7% (197) had UC-related surgery in the past 5 yrs, with an average of 2.3 surgeries per respondent. The mean time from diagnosis to first surgery was 39.6 months. Of the respondents who had undergone surgery, 37.1% had their entire colon removed and 31% reported that they were required to wear an ostomy bag. Almost equal percentages of respondents indicated that their lives were better before surgery as opposed to better after surgery (49.2% vs. 45.0%). This was also true for those who had a total colectomy (32.6% vs. 30.4%). However, QOL was still affected by UC following surgery (Table). Pts who had undergone surgery also reported a substantial number of workdays missed (9.3 in the past 30 days) and less productive workdays (24.7 in the past 30 days) due to UC symptoms.

Mean number of days in the past 30 days with UC-related symptoms

Because of UC, during the past 30 days, how many days...	UC Surgery Other than Total Colectomy	Total Colectomy
Did PAIN make it hard for you to do your usual activities, such as work or recreation?	9.8	8.6
Have you felt SAD, BLUE, or DEPRESSED?	8.6	8.5
Have you felt WORRIED, TENSE, or ANXIOUS?	10.6	10.0
Have you felt you did NOT get ENOUGH REST or SLEEP because of your UC?	12.1	10.9
Have you felt STRESSED?	13.8	12.1

**Conclusion:** Almost 20% of respondents reported having surgery for UC, and those who had surgery still reported feelings of pain, depression, anxiety, sleeplessness and stress due to their disease. Work life following surgery was still negatively affected. Further studies are needed to better understand optimal management and outcomes in UC.

866

### Infliximab Is Clinically Effective in Reducing the Need for Steroids in Inflammatory Bowel Disease

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**Purpose:** To determine the influence of infliximab (IFX) on steroid use in pts with inflammatory bowel disease (IBD), including Crohn's disease (CD) and ulcerative colitis (UC).

**Methods:** A retrospective analysis was conducted using medical and pharmacy claims from the PharMetrics database btw Jan. 1, 2000 and June 30, 2005. Pts were required to have 2 distinct claims for CD (ICD-9 codes 555.x) or UC (ICD-9 codes 556.x) and were limited to those started on IFX therapy before June 30, 2004. Corticosteroid use was evaluated 12 mos before and 12 mos after the first IFX claim (IFX index date). Continuous enrollment was required. Outcomes of interest included: the % of pts with at least 1 prescription for an oral steroid; mean number of steroid prescriptions per pt; and mean number of days in which a steroid was theoretically available per pt. Basic population characteristics were examined including demographics and overall pt comorbidity burden (Charlson Comorbidity Index).

**Results:** Of the 971 CD pts and 274 UC pts that received IFX, over half of the pts were female and the mean age was 40 for CD and 39 for UC. The mean Charlson Comorbidity Index score was 1.9 for CD and 2.4 for UC. In the yr prior to the IFX index date, 58.6% (569) of pts with CD had a prescription for an oral steroid vs 45.1% (438) in the yr following the index date ( $P < 0.05$ ). In the yr prior to the IFX index date, 69.7% (191) of pts with UC had a prescription for steroids vs. 52.1% (143) in the yr following the index date ( $P < 0.05$ ). Significant reductions in the mean number of corticosteroid prescriptions for both CD (2.5 vs 1.8;  $P < 0.05$ ) and UC (1.9 vs 1.4;  $P < 0.05$ ) and the number of days in which a corticosteroid was available for CD (70.3 vs 48.6;  $P < 0.05$ ) and UC (49.9 vs 36.2;  $P < 0.05$ ) were documented during the post-IFX period.

Steroid use pre- & post-IFX

	CD		UC	
	Pre-IFX	Post-IFX	Pre-IFX	Post-IFX
% of pts with steroid prescription	58.6(569)*	45.1(438)*	69.7(191)*	52.1(143)*
Mean # of steroid prescriptions	1.9(2.5)**	1.4(2.4)**	2.5(2.6)**	1.8(2.6)**
Mean # of steroid days	49.9(73.1)**	36.2(69.7)**	70.3(82.6)**	48.6(72.4)**

\* $P < 0.05$  chi square test \*\* $P < 0.05$  paired t-test

**Conclusion:** This analysis indicated that IFX use resulted in a reduction in overall corticosteroid use in pts with IBD. Consequently, use of IFX should be considered for IBD pts who are dependent on corticosteroids, have steroid toxicity, and who are not responding adequately to treatment with steroids.

867

### The Pre-Operative Utility of Dobutamine Stress Echocardiography in Patients Undergoing Liver Transplantation

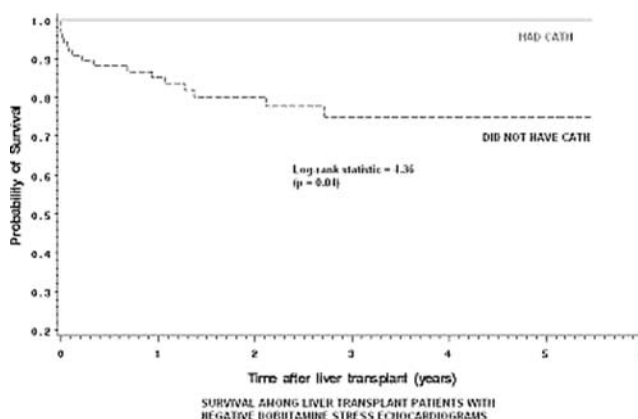
Lynn Shapiro, MD, Maximilian Lee, MD, Jason Lee, MPH, Alex S. Lapasaran, MSN, APN, William Fearon, MD, Ahmad Kamal, MD, MSc, Aijaz Ahmed, MD\*. Division of Gastroenterology and Hepatology, Liver Transplant Program, Stanford University School of Medicine, Stanford, CA; Center for Primary Care and Outcomes Research, Stanford University School of Medicine, Stanford, CA; Division of Cardiovascular Medicine, Stanford University School of Medicine, Stanford, CA and Division of Gastroenterology, Santa Clara Valley Medical Center, San Jose, CA.

**Purpose:** To determine whether dobutamine stress echocardiography (DSE) is sufficient to rule out significant coronary artery disease (CAD) in patients undergoing liver transplantation (LT).

**Methods:** At our institution, 281 adults underwent LT between January 1, 2000 and June 30, 2006. Pre-operative DSE was performed in 121 (43%) out of 281 adult LT recipients to screen for CAD. Patients (N = 121) who underwent DSE were either >50 years in age and/or with presence of 1 or more major cardiac risk factors. We conducted a retrospective review of any subsequent angiography and survival.

**Results:** 109 (90%) patients had a normal DSE and 12 (10%) patients had an abnormal DSE, including 3 with stress-induced wall motion abnormalities and 9 with resting wall motion abnormalities. Coronary angiography was performed in 24 patients with a normal DSE: 6 patients were found to have significant lesions and 4 required intervention. Angiography was also performed in 4 patients with an abnormal DSE: only 1 patient had a significant lesion and it required intervention. DSE had 14% sensitivity and 85% specificity for CAD, with 25% positive predictive value and 75% negative predictive value. After a median follow-up of 1.8 years (range, 0 to 5.5 years), survival was higher in those patients who had undergone coronary angiography despite a normal DSE, than in those were assumed to have no CAD based on a normal DSE alone (100% versus 80%,  $P = 0.04$ ).

**Conclusion:** A normal DSE may be insufficient in ruling out CAD in high risk patients undergoing LT. The lower mortality in those patients who underwent angiography despite a normal DSE suggests that significant lesions may be missed with non-invasive testing and that cardiac intervention prior to transplant may improve outcomes.[figure1]



868

### An Exploratory Analysis of Healthcare Utilization and Costs in Pediatric Crohn's Disease

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**Purpose:** To evaluate healthcare utilization costs associated with pediatric Crohn's disease (PCD) from a payor perspective.

**Methods:** An analysis using data from 2003 through 2006 containing claims for HMO pts assigned to HealthCare Partners Medical Group from 6 commercial health plans in S. CA was conducted. Newly diagnosed pts age <18 with Crohn's disease (CD; ICD-9 555.x) were identified. Pts were required to have 6-mos pre- and 12-mos post continuous eligibility from their disease index date. Cost and resource utilization were compared to a cohort without CD who were matched to the pts with PCD on age, sex, and birthday (within 30 days of age/sex matched pts with PCD). Statistical significance was not assessed due to the small sample size.

**Results:** 62 pts with PCD were identified, with 30 meeting the continuous eligibility criteria. Most were female (56.7%) and the median age at dx was 13 yrs. The comparator grp consisted of 10,864 children. The total per member per month (PMPM) cost for pts with PCD was \$2,547.32, with 70% attributable to PCD, vs a PMPM cost of \$166.07 for the non-PCD cohort. There were 500 admissions per 1,000 members per yr (PTMPY) for the PCD grp vs 11.2 for the comparator cohort. The average length of stay (ALOS) was also longer for the PCD cohort (7.6 days vs 4.4 days). The PMPM cost of inpt stays was \$1,409.41 for the PCD cohort vs \$18.16 for the comparator cohort.

**Conclusion:** PCD is associated with much higher levels of resource utilization and costs of care, primarily driven by inpt stays. Treating PCD appropriately before the disease progresses to a level requiring hospitalization may help reduce some of the costs in PCD.

Costs \$	PCD		Comparator Total PMPM
	Total PMPM	% with PCD Dx	
Outpt Office Visits	106.06	50	13.91
Outpt Office-Based Procedures	28.24	96	5.10
ER	69.15	61	6.12
Day Surgery	544.30	89	0.83
Lab	44.53	28	2.67
Inpt	1,409.41	75	18.16
Pharmacy	293.13	32	18.32
Total	2,547.32	70	166.07
Utilization	Total PTMPY	% with PCD Dx	Total PTMPY
Outpt Office Visits	10,733	47	1,971.2
Outpt Office-Based Procedures	2,000	52	293.7
ER	400	75	72.6
Day Surgery	1,800	65	0
Lab	13,000	39	1,034.3
Inpt Admits	500	73	11.2
Inpt ALOS	7.6		4.4
ALOS-PCD Admits	7.8		N/A
ALOS-Non-PCD Admits	7.0		N/A
Pharmacy (Per Member Per Year)	20.3	30	2.3

## 869

### Current Physician Extender Utilization Patterns in Community Based GI Practice

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**Purpose:** Various pressures in medicine demand increased efficiency of GI patient care models. Physician extenders Nurse Practitioners (NP) and Physician Assistants (PA) have become essential components in both the inpatient and outpatient setting. There is a lack of useful data regarding extender use pattern in community based GI practices.

**Methods:** Extender use was compared between two busy active gastroenterology practices in different geographic locations within the U.S.

**Results:** Huron Gastroenterology (HG) is a 13 physician practice. This practice utilizes 5 physician extenders (4 PA's and 1 NP's). HG uses one PA exclusively in the hospital, 3 PA's in the office and hospital, and the NP is dedicated to a liver clinic. The Center of Digestive and Liver Health (CDLH) is an 8 physician practice utilizing 7 physician extenders (3 NP's

and 4 PA's). One extender is assigned to inpatient services. 3 extenders are assigned to assist the primary physician in the office. One extender is assigned to see urgent follow up patients who have called seeking care. One NP is dedicated to pediatric gastroenterology. The last extender covers extender vacations and, also, assists with urgent care. CDLH does not currently utilize physician extenders for on call coverage or weekends. Pay range is from 57K-82K depending on experience at both locations. The ratio of physicians to extenders varies between these two groups due to group preference (HG: 5 extenders/13 MD's (38.7%), CDLH: 7 extenders/8 MD's (87.5%).

**Conclusion:** Physician extenders may be utilized in all non-endoscopic phases of community based GI practice to improve access for patients and facilitate care, yet little data is readily available. As demand for endoscopic services increases, the utilization of extenders may increase. Salaries for experienced extenders are considerable, but generally, the cost is made up via increased patient volume and subsequent revenue. More widely disseminated information would be useful for GI practices to make informed decisions regarding the optimal number and utilization of physician extenders, thereby enhancing practice efficiency and improving patient care delivery. Prospective studies of quality of care rendered, reimbursement for services, and patient satisfaction will be beneficial to practices considering expanding the role of physician extenders in practice.

## 870

### Management of Iron Deficiency Anaemia: Are We Meeting the Guidelines?

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**Purpose:** Iron deficiency anaemia (IDA) accounts to upto 15% of all referrals to gastroenterologists. In spite of the availability of well established guidelines the management of IDA is often suboptimal with most patients, if not at all being incompletely investigated. The diagnostic criteria for IDA vary between published studies. This study was done to review the management of patients with IDA at a district general hospital in UK and determine the pitfalls in the diagnosis and treatment of these patients.

**Methods:** A proforma was devised based on the guidelines laid by the British Gastroenterology Society (BSG) for the management of IDA. Retrospective review of case notes of all patients with a new diagnosis of IDA between January 2005 and December 2006 was carried out. Patients with obvious source of blood loss (melaena, haematemesis, PR bleed) were excluded from the study. Elderly and infirm patients who were deemed to be not fit for further investigations were also excluded from the study.

**Results:** This retrospective study included 110 patients (24 male, 66 female) with age ranging from 22 yr-80 yr (median age 66 yr). About a third of the patients (29%) presented with gastro-intestinal (GI) symptoms. A majority of the patients (47%) were asymptomatic and IDA was diagnosed following routine blood tests. In 38% of the patients IDA was secondary to GI causes. Non GI causes like menorrhagia, epistaxis, mechanical heart valve attributed to 12% of cases. 24% of patients with a normal upper GI endoscopy were discharged without any lower GI investigations. In 18% of patients no further investigations were arranged after a normal upper and lower GI endoscopy. 20% patients found to have refractory anaemia were referred to specialist centres for further investigation. Most of the patients were managed medically with oral iron (96%) and parenteral iron (29%) therapy. 24% patients received blood transfusion, two thirds of which were not indicated as per hospital blood transfusion guidelines. Long term proton pump inhibitor therapy was indicated in 49% of patients but was prescribed in only 30% of the patients.

**Conclusion:** Overall adherence to the BGS guidelines was poor. A care pathway to guide physicians for investigating and treating patients with iron deficiency anaemia was recommended. If a GI cause for IDA is not found after a bidirectional endoscopy then it is necessary to proceed with further investigations to look for non GI causes.

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### Does FNA Improve the Accuracy of Endoscopic Ultrasound in Evaluating Mediastinal Lymphadenopathy? A Meta-Analysis and Systematic Review

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**Purpose:** The published data on accuracy of endoscopic ultrasound (EUS) to differentiate inflammatory from neoplastic process in a lymph node has been varied. This differentiation is crucial for appropriate therapy. The impact of EUS-fine needle aspiration (FNA) in the evaluation of mediastinal lymphadenopathy is not clear.

**Aim:** To evaluate the accuracy of EUS alone and EUS with FNA in evaluating mediastinal lymphadenopathy

**Methods: Study Selection Criteria:** Only EUS and EUS-FNA studies confirmed by surgery or with prolonged follow-up were selected.

**Data collection & extraction:** Articles were searched in Medline, Pubmed, Ovid journals, CINAHL, and Cochrane controlled trials registry. Two reviewers independently searched and extracted data. The differences were resolved by mutual agreement.

**Statistical Method:** Meta-analysis for the accuracy of EUS was analyzed by calculating pooled estimates of sensitivity, specificity, likelihood ratios, and diagnostic odds ratios. Pooling was conducted by both fixed and random effects models.

**Results:** Initial search identified 3610 reference articles, in which, 460 relevant articles were selected and reviewed. Data was extracted from 76 studies (N = 9310) which met the inclusion criteria. Of these, 44 studies used EUS alone and 32 studies used EUS-FNA. The pooled estimates are shown in table 1. All the pooled estimates, calculated by fixed and random effect models, were similar. The *P* for chi-squared heterogeneity for all the pooled accuracy estimates was > 0.10.

**Conclusion:** EUS appears to be a good diagnostic tool to evaluate mediastinal lymphadenopathy. This meta-analysis shows that FNA substantially improves the accuracy of EUS in evaluating mediastinal lymphadenopathy. EUS with FNA should be the diagnostic test of choice in evaluating mediastinal lymphadenopathy.

**Table 1.** Showing the pooled estimated for accuracy of EUS and EUS-FNA in evaluating Mediastinal Lymphadenopathy with 95% confidence intervals.

	EUS	EUS-FNA
Studies	44	32
Pooled sensitivity	84.7% (82.9–86.4)	88.0% (85.8–90.0)
Pooled specificity	84.6% (83.2–85.9)	96.4% (95.3–97.4)
Positive likelihood ratio	3.3 (2.6–4.3)	11.2 (5.9–21.2)
Negative likelihood ratio	0.24 (0.9–0.3)	0.1 (0.1–0.2)
Diagnostic odds ratio	19.1 (12.7–28.5)	106.9 (54.4–210.3)
Area under the curve	0.91	0.97

872

### Diagnostic Accuracy of Endoscopic Ultrasound in Detecting Distal Metastasis of Esophageal Cancers: A Meta-Analysis and Systematic Review

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**Purpose:** Distal metastasis in patients with esophageal cancer predicts prognosis and guides therapy. The published data on accuracy of endoscopic

ultrasound (EUS) for diagnosing distal metastasis (M1) in patients with esophageal cancer has been inconsistent.

**Aim:** To evaluate the accuracy of EUS in diagnosing distal metastasis of esophageal cancers.

**Methods: Study Selection Criteria:** Distal metastasis was defined as metastasis to peritoneum, liver, cervical lymph nodes, celiac axis lymph nodes, or abdominal lymph nodes. Only EUS studies confirmed by surgery were selected. EUS criteria used for nodal invasion were: larger than one centimeter, hypoechoic, and round.

**Data collection & extraction:** Articles were searched in Medline, Pubmed, Ovid journals, and Cochrane controlled trials registry. Two reviewers independently searched and extracted data. The differences were resolved by mutual agreement.

**Statistical Method:** Meta-analysis for the accuracy of EUS was analyzed by calculating pooled estimates of sensitivity, specificity, likelihood ratios, and diagnostic odds ratios. Pooling was conducted by both fixed and random effects models. The heterogeneity among studies was tested using Cochran's *Q* test based upon inverse variance weights.

**Results:** Initial search identified 2630 articles, in which, 336 relevant articles were selected and reviewed. Data was extracted from 25 studies (N = 2029) that met the inclusion criteria. Pooled sensitivity of EUS in diagnosing nodal involvement by esophageal cancers was 67.2% (95% CI: 62.6–71.6). EUS had a pooled specificity of 97.9% (95% CI: 97.1–98.6). The positive likelihood ratio of EUS was 18.5 (95% CI: 10.1–33.9) and negative likelihood ratio was 0.3 (0.2–0.5). The diagnostic odds ratio, the odds of having metastasis in positive as compared to negative EUS studies, was 68.9 (35.4–134.1). All the pooled estimates, calculated by fixed and random effect models, were similar. SROC curves showed an area under the curve of 0.91. The *P* for chi-squared heterogeneity for all the pooled accuracy estimates was > 0.10.

**Conclusion:** This meta-analysis shows that EUS has a high specificity but low sensitivity to evaluate distal metastasis of esophageal cancers. Improvements in technology or diagnostic criteria are needed to enhance the sensitivity.

873

### Efficacy of Proton Pump Inhibitors in Reflux Laryngitis: A Meta-Analysis and Systematic Review

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**Purpose:** Gastro-esophageal reflux disease (GERD) can present with atypical manifestations such as reflux laryngitis (RL). Patients with RL may have symptoms like hoarseness, chronic throat clearing, and excessive phlegm and laryngoscopy shows findings indicating posterior laryngeal inflammation. The efficacy of proton pump inhibitors (PPI) for resolution of laryngeal symptoms and laryngoscopic findings in RL pts has been varied. The aim of this meta-analysis was to determine the efficacy of PPI's in RL.

**Methods:** We searched for articles in Medline, Pubmed, Ovid journals, and Cochrane controlled trials registry. Only randomized, double-blind, and placebo-controlled trials were selected. Pts selection criteria included: age 18 to 80 yrs, use of twice daily PPIs, with symptoms suggestive of RL and laryngoscopic signs of inflammation, dual probe pH testing documenting acid reflux, no acid suppressive therapy 2 wks prior to start of trial and treatment for a minimum of 8 to 12 wks.

**Statistics:** Pooled effect sizes for mean difference in symptom scores and laryngoscopic scores were calculated by both fixed and random effect models. Pooled effect size was expressed as weighted mean difference (WMD).

**Results:** 6 randomized, placebo-controlled trials met the study criteria. Of these, 5 studies (N = 167) reported a mean score of symptoms and laryngoscopic findings and were included in this analysis. Treatment follow-up

periods were 16 weeks in 1 study, 12 weeks in 2 studies and 8 weeks in the remaining two studies. The WMD between PPI and placebo for laryngeal symptoms was -0.467 (95% CI = -3.40 to 2.47; test of heterogeneity,  $P = 0.76$ ). The pooled estimate of WMD in laryngoscopic scores between PPI and placebo was 0.157 (95% CI = -0.101 to 0.414; test of heterogeneity,  $P = 0.98$ ). I statistic gave a 0% inconsistency (95% CI = 0% to 64.1%). Publication bias calculated using Begg-Mazumdar bias indicator gave a Kendall's b tau value of 0 ( $P = 0.82$ ) and Egger bias indicator gave a value of -0.12 (95% CI = -1.40 to 1.1,  $P = 0.81$ ).

**Conclusion:** Twice daily PPI therapy leads to an improvement in the mean scores of both laryngeal symptoms and laryngoscopic scores, but the differences are not significant when compared to placebo. There is a large placebo effect in patients with RL. Better risk stratification of RL patients including improved diagnostic tools are needed for this group of patients.

## 874

### Impact of Post-Operative Ileus (POI) on Hospital Length of Stay in Colectomy Surgery Patients

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**Purpose:** To study the impact of postoperative ileus (POI) on hospital length of stay in colectomy patients.

**Methods:** A retrospective cohort study design was used. Adult patients with a principal procedure code for partial excision of large intestine (ICD-9 code: 45.71-45.79), discharged between Jan 2004-Dec 2004 were identified from Premier's Perspective Comparative Database, an inpatient records database from over 500 hospitals in the United States. The colectomy patients were further classified for the presence of POI, by the presence of paralytic ileus (ICD-9 code 560.1) and/or digestive system complications (ICD-9 code 994.1) during the study period. Multivariate hierarchical regression analysis was performed with log-transformed length of stay as the dependent variable. Patient demographics, mortality risk, disease severity, admission source, payment type, and hospital characteristics were used as covariates.

**Results:** A total of 17,896 patients with a primary procedure code for colectomy were identified, of which 3,115 (17.4%) patients had a secondary diagnosis of POI, including paralytic ileus ( $N = 2,732$ ; 15.3%) and digestive system complications ( $N = 1,899$ , 10.6%), with significant overlap between the two ( $N = 1516$ , 8.5%). The majority of colectomy patients with POI were male (54.9%), Caucasian (70.9%) and in the 51-64 year age group (51%). The crude average hospital length of stay was significantly higher ( $P < 0.001$ ) in colectomy patients with POI ( $13.75 \pm 13.33$  days) compared with patients without POI ( $8.85 \pm 9.49$  days). Presence of POI was found to significantly increase hospital length of stay (antilog  $b = 1.29$ ,  $P < 0.001$ ) in the regression model. Gender ( $P < 0.01$ ), severity level ( $P < 0.001$ ), admission source ( $P < 0.05$ ) and hospital size ( $P < 0.05$ ) were other significant predictors of hospital length of stay.

**Conclusion:** Postoperative Ileus (POI) is associated with a significant increase in the hospital length of stay in colectomy patients. Prevention of POI in colectomy patients could potentially decrease hospital length of stay and reduce costs.

## 875

### Long-Term Outcomes of H. Pylori Infection That Was Undiagnosed or Untreated at First EGD

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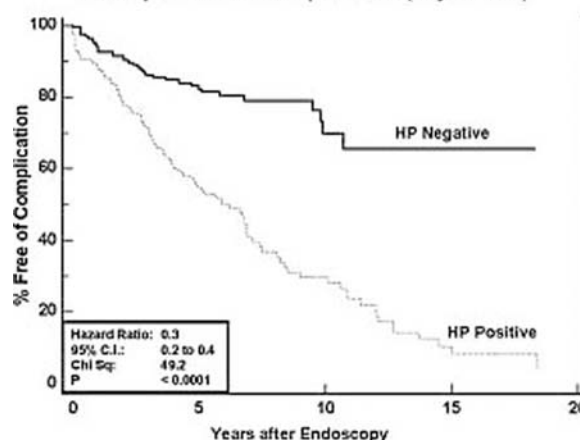
**Purpose:** Patients with GI Sx are treated with PPI's, scheduled for EGD, scoped at a later date, and invariably found to have a "normal" exam. Bx for

H. pylori (HP) infection is not routine. If HP is present, the patient will not know from the EGD. We claim that ignoring potential HP infection allows survival of HP sleeper-cells, which may in due course result in HP terror attacks. The purpose of this study is to investigate the validity of that claim. **Methods:** The At-Risk Study Group comprises outpts that had EGD with gastric Bx at any time during a 4-yr Recruitment Period (RP) from Jan-1998 through Dec-2001. The Study Group was formed from 2 pathways: (1) Pts who had EGD *before* the RP and again later *in* the RP [Began with EGD before the RP]; and (2) Pts who had EGD *in* the RP and then again later some time *in the future* [Began with EGD in the RP].

**Results:** The At-Risk Study Group comprises 1207 pts with gastric Bx: 408 have known outcomes (good and bad) and 799 have yet to declare themselves. HP-Pos pts had worse outcomes in all parameters. HP-Pos pts had 3.3 $\times$  greater risk of "any" (major or minor) complications (Hazard Ratio = 0.3; CI:0.2-0.4;  $P < 0.0001$ ), 5.6 $\times$  greater risk of "major" complication, and 1.3 $\times$  greater "all-cause" mortality. Age, NSAIDs, H2RAs (Multiple Regression) did not contribute to outcome. PPIs were protective (OR = 3.1).

**Conclusion:** In Pts having EGD for any reason, the failure to diagnose silent HP infection or the failure to treat those patients who tested positive exposes patients in the decade to come to a 5-6 $\times$  greater frequency of major GI complications.[figure1]

### Continued HP Infection After a Previous EGD Subsequent Risk of Complications (Major/Minor)



### Long-Term Complication Rate of HP Neg and Untreated HP Pos

	Any Complication	Major Complication	All-Cause Mortality
HP-Pos	55.9%	26.3%	29.9%
HP-Neg	18.7%	4.4%	20.2%
Diff (95% CI)	37.2% (CI: 30%-40%)	21.9% (CI: 14%-38%)	9.7% (CI: 1.4-18%)
P-Value	<0.0001	<0.0001	= 0.03

## 876

cag PAI in *H. pylori* Isolated from Dyspeptic Patients in Tehran, Iran  
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**Purpose:** The aim of this study was to investigate the prevalence of *cagPAI* in *H. pylori* isolated from gastritis patients in Tehran, Iran.

**Methods:** A total of 70 *H. pylori* strain with positive PCR results for *glmM* gene were selected from dyspeptic patients in Tehran, Iran. DNA extraction from biopsies was performed by QIAamp<sup>®</sup> DNA Mini Kit (QIAGEN GERMAN). PCR amplification was used for four loci (*cagA*, *cagG*, *cagM*, *cagT*) of *cag PAI*.

**Results:** Out of 70 biopsy samples with *glmM*-positive gene, *cagA* were detected in 74.3% (52 of 70) of patients. The prevalence of *cagT*, *cagG* genes were 15%, 10% respectively. *cagM* gene was not detected in studied isolates. Co-existence of *cagA/cagT*, and *cagA/cagG* were detected in 12 and 7 isolates respectively. We detected 6 *H. pylori* isolates with *cagA* negative; however they carried either *cagG* or *cagT* genes. There were 4 isolates which had three genes (*cagA/cagG/cagT*) together.

**Conclusion:** The pathogenic role of the *cag PAI* as a whole or in part, in disease development, is not yet completely understood. Although the most studies were reported that there are correlations between genotyping of *cagPAI* and PUD or GC. Finding of this study showed all of isolates from NUD patients were carried at least one of *cagG/cagT/cagA* genes. According to result, the *cagA* gene could be served as a better marker for the *cag PAI*. However, the presence of this single gene does not necessarily indicate the presence of a complete set of *cag PAI* genes. Low prevalence of PUD samples may relate to lack of *cagM*, whose product is essential for type IV secretion system. At the end we suggest studding of more genes of *cagPAI* in patients with PUD and gastric cancer in large population.

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#### Prevalence of Gastrointestinal Symptoms and the Influence of Demographic Factors

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**Purpose:** In this study, we obtained the prevalence of some important gastrointestinal symptoms such as nausea, vomiting, rectal bleeding, anorexia, and weight loss which may point to a structural GI disease. The prevalence of some of gastrointestinal symptoms relevance with demogrpch factors.

**Methods:** This is a cross- sectional study with a reliable questionnaire that was performed during six months in 2006, on random sampling of 1304 people of Tehran. After interviews one physician was consulted for symptoms in respondents. We invited people for an interview and a clinical examination. Questionnaire was completed in two urban and rural areas.

**Results:** Mean age of the responders was  $34.8 \pm 16.6$  years (range 12–70). A mean of 19.6% of subjects reported experiencing at least one of the 11 GI symptoms. Women were significantly more than men to experience relevant symptoms. Overall, 100,000 of Iranian population (48.7% men and 51.3% women). Mean age of the responders was  $34.8 \pm 16.6$  years (range 12–70). Prevalence of gastrointestinal symptoms included: abdominal pain was 10.1%, constipation 6.2%, diarrhea 1.1%, abdominal bloating 10% dyspepsia 11.3% proctalgia 1.5%, nausea and vomiting 1.2%, incontinence 0.5%, GI bleeding 0.7%, weight loss 0.9% dysphagia 0.6%. Some of gastrointestinal symptoms were common in married as dyspepsia 14.5%, abdominal bloating 13.2%, abdominal pain 13%, constipation 8.3%, incontinence 0.5%. We obtained relevance between education & gastrointestinal symptoms as dyspepsia increased by education: Primery 18.9%, lowerdiploma 10.5%, diploma 9%, upper diploma 6.5%, Ms or upper 0%. In these population 12–35 age group was 42.9% and 36–70 age group was 57.1%. All of GI symptoms are common in those of >35 years except diarrreh, vomiting, incontinence.

**Conclusion:** Dyspepsia is the most common (M = F = 11.3%). Constipation (F = 7.6% & M = 4.7%) and proctalgia (F = 2.1% & M = 0.8%) are common in female (*P*-value < 0.05), and other symptoms are statistically equal in both female and male. Dyspepsia and constipation are common in >35 years of female and male but in female is more. Gastrointestinal symptoms and symptom complex are common in older people in Iran community. Gastrointestinal symptoms were common in married and low education. It is no relevance between insurance and gastrointestinal symptoms in this study.

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#### The Role of *cagE*, *oipA*, *cagA* and *vacA* Genes of *Helicobacter pylori* in Iranian Dyspepsia Patients

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**Purpose:** The aims of this study was determination of the association between the *cagE*, *oipA*, *cagA*, *vacA*, genes and clinical manifestations.

**Methods:** A total of 60 gastric biopsies from 60 patients who were qualified for endoscopies of the upper gastrointestinal were included in this study. The genomic DNA was extracted from biopsy samples by Qiagen tissue kit. The status of the *cagE*, *oipA*, *cagA*, *vacA* genes was studied by using the polymerase chain reaction (PCR) method.

**Results:** In all of selected specimens, *glmM* gene was used as a screening test for confirmation of *Helicobacter pylori*. *cagA*, *cagE*, and *oipA* genes were present in 42(70%), 17(28%), and 37(61%) of 60 samples respectively. 11 (18.3%) of patients were classified in PUD group and 49(81%) were in NUD group. in PUD patients, 5(45%) were positive for *cagA* whereas 6(54%) were positive for *cagE*. five of ulcerative samples have *oipA*. genes. Interestingly all of *cagA* positive samples were positive for *cagE* and *oipA* too. All of ulcerative samples were *vacA* m2 positive. s1m2 was predominant genotype in all PUD patients.

**Conclusion:** Current study demonstrated high frequency of *cagA* and low prevalence of *cagE* in studied samples which shows may in spite of some other studies, *cagA* is better marker of *cagPAI* than *cagE*. Since *cagE* was positive in 54% of PUD in compare to 22% in NUD patients, this study suggest that presence of *cagE* is better probe for prognosis of ulcer formation. Overall we conclude presence of *cagE* and *oipA* beside of *vacA* s1m2 may be helpful in prediction of ulcer formation in *H. pylori* infected patients. Finally we suggest performing this kind of study in large scale.

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#### Clinical Outcomes of *Helicobacter pylori* Infection in Relation to *vacA* and *cagA* Genotypes in Iranian Patients

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**Purpose:** The aims of this study were to evaluate the role of *vacA* genotyping with respect to gastric inflammation and injury, and clinical presentation in Iranian populations.

**Methods:** Genomic DNA from biopsy specimens from patients with gastritis, peptic ulcer disease and gastric cancer were characterized by *ureC* (*glmM*), *cagA* and *vacA* genotyping by polymerase chain reaction (PCR).

**Results:** Our results showed that 96 (57%) of 167 patients with gastro duodenal diseases, 19 of 33 gastroduodenal ulcer and 3(60%) of 5 gastric cancer were infected with *H. pylori*. In this study 19.8% strains were isolated from patients with PUD and 68.7% from patients with NUD.s1m2 genotype was observed in 36.8%, of PUD and 40.5% NUD patients.

**Conclusion:** Prevalence of cagA positive (76%) in Iran is close to that of Europe and North America (60–70%) than Asian countries (90%). Regarding the vacA gene, 97% (93 of 96) of *H. pylori* positive patients determined by ureC (glmM) PCR were successfully detect the vacA gene. The vacA s1m2 was predominant genotype in Iran (41%). The prevalence of s2m1 (8.3%) was high in Iranian isolates. Although individuals who infected with *H. pylori* possessing the cagA (+) gene and vacA m2 genotypes were more sensitive to development of gastroduodenal disease but we could not find any significant correlation between cagA status and PUD, because of similar high cagA gene positivity in the *H. pylori* strains isolated from PUD (78.6%) and NUD (74.3%). CagA status cannot be used as a useful marker to predict the outcome of the infection in patients in Iran.

## 880

### Non-Cutaneous Head and Neck Cancer in Solid Organ Transplant Recipients

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**Purpose:** Head and neck cancer is the most common site of cancer in the transplant population. The goal of this study was to examine the nature and behavior of non-cutaneous head and neck cancer (NCHNC) in solid organ transplant recipients at the University of Tennessee Health Science Center.

**Methods:** Cases of post transplant de novo non-cutaneous head and neck cancer diagnosed between 1995 and 2002, were compared with the general population (SP) using data from the National Cancer Institute.

**Results:** During the 8 year period, 1120 solid organ transplantation (TXP) were carried out. Six cases of NCHNC were identified. The incidence of SCC of the head and neck was 0.5% (6/1120). 5/6 patients had history of smoking and 5/6 of post-transplant diabetes mellitus. The median age at TXP was 51 years (41 to 59 years). 5/6 patients were Caucasian and 1/6 African-American. 5/6 patients were male and 1/6 female. The median time to first diagnosis of cancer was 2.5 years (4 months to 13 years) after TXP. NCHNC was the first de novo cancer in all patients. All the patients died. 4/6 patients died of causes related to non-cutaneous head and neck cancer and 2/6 died of other cancers. The median survival after diagnosis of cancer was 14.7 months (90 days to 2.9 years). The median age at diagnosis of NCHNC in the GP was 62.8 years and survival after diagnosis was 26 months. Although the median age at diagnosis of NCHNC is not statistically different from the GP ( $P$  value = 0.156), the survival curve of these patients is poor compared to the GP ( $P$  value = 0.0217).

**Conclusion:** Although, the incidence NCHNC was 0.5%, it was the first post-transplant malignancy to be diagnosed in all our cases. History of smoking and post-transplant diabetes was commonly found in NCHNC in solid organ transplant recipients. These patients should undergo routine screening for NCHNC, which if occurs may be the first post-transplant malignancy in these patients, has a shorter survival and higher mortality compared to the GP.

## 881

### Statin Use and the Risk of Colorectal Cancer in Patients with Diabetes

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**Purpose:** Colorectal cancer (CRC) is one of the leading causes of cancer deaths worldwide. Experimental data indicate a possible prevention effect for statins in CRC. However, the available epidemiological data are conflicting.

**Methods:** We conducted a nested case-control study within a cohort of veterans with diabetes identified by ICD 9 codes or medication use in national VA databases. The records were also linked to Medicare files to maximize the probability of capturing health care encounters among dual VA-Medicare users. Cases were defined as incident CRC during 1/2001–12/2002 without prior history of lung, pancreas, stomach, esophagus, breast, or liver cancer prior to index date. Cases were individually matched on age and incidence density to four controls without CRC. Patients with incomplete Medicare enrollment, HMO-Medicare enrollment, or no VA pharmacy use were excluded. VA Pharmacy Benefits Management files were used to identify filled statin prescriptions including type, dose, and duration. Multivariable conditional logistic regression models were used to estimate odds ratios after adjusting for confounding variables.

**Results:** The cohort comprised of 763,807 veterans with diabetes. A total of 6080 cases and 24,320 matched controls were examined. The mean age was 74 and the majority of patients were Caucasian (88%) and/or male (99%). The mean duration between entry into cohort and CRC index date was 2.3 years. Filled statin prescriptions were recorded less frequently in cases (49%) than in controls (52%); OR, 0.88; 95% CI 0.83–0.93. This inverse association remained significant after adjusting for inflammatory bowel disease, severity of diabetes, cholecystectomy, liver disease, use of aspirin or NSAIDs, or colon evaluation by endoscopy, imaging, or fecal occult blood testing. Longer durations of filled statin prescriptions were associated with greater risk reduction in CRC: OR, 0.89; 0.84–0.94 (6 months), OR, 0.86; 0.81–0.92 (12 months), OR, 0.85; 0.79–0.91 (18 months), OR, 0.83; 0.76–0.90 (24 months). Simvastatin comprised the majority of statin use (87%) and the findings were very similar to those of any statin. No significant associations were observed between CRC and non-statin cholesterol (OR, 1.02; 0.88–1.18) or triglyceride lowering medications (OR, 0.96; 0.87–1.05).

**Conclusion:** The use of statins was associated with a significant reduction (~10%) in the risk of CRC in patients with diabetes. This risk reduction seems to be greater in patients with longer duration of statin use.

## 882

### Influence of Esophagogastroduodenoscopy (EGD) on Prescription (Rx) Fill Patterns for Proton Pump Inhibitors (PPIs) and Nonselective Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) among Type-2 Diabetic (T2D) and Nondiabetic Patients

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**Purpose:** To examine the effect of EGD on Rx fill patterns for PPIs and nonselective NSAIDs in T2D and nondiabetic patients.

**Methods:** Data on patients aged  $\geq 18$  y in the MarketScan administrative claims database with full enrollment data for 180 d pre- and post-EGD from 2000–2005 were extracted (D9612L00108). EGD was identified by CPT codes; T2D patients were identified as having  $\geq 2$  medical claims for T2D by ICD-9 codes or  $\geq 2$  oral antidiabetic Rx; and nondiabetic patients were identified as having no ICD-9 codes for any type of diabetes or Rx for antidiabetic medications. PPI and nonselective NSAID use were defined by national drug codes. T2D patients who underwent EGD were matched 1:1 with nondiabetic patients by age and gender. McNemar's test was used for proportion differences pre- and post-EGD;  $\chi^2$  tests were used for differences between independent cohorts.

**Results:** Of the 10,546,828 patients in the MarketScan database, 9,373,650 had no diabetes; 953,766 had T2D; 219,412 had other types of diabetes. In the matched population ( $N = 39,636$  for each group), post-EGD, Rx fills increased for PPIs and decreased for nonselective NSAIDs (Table). Among patients already taking PPIs, 80.3% continued to use them post-EGD. Among patients not taking PPIs pre-EGD, 38.3% began using them post-EGD. The percentage of patients adding a PPI post-EGD was higher ( $P < .0001$ ) for patients using (44.6%) than not using nonselective NSAIDs

(37.9%). Of patients who took nonselective NSAIDs, 56.7% discontinued use post-EGD, and this proportion was lower ( $P < .0001$ ) in patients who took (52.4%) than those who did not take concomitant PPIs (59.9%). No meaningful differences were seen between the T2D and nondiabetic groups. **Conclusion:** PPI use increased and nonselective NSAID use decreased post-EGD. Most patients who took only a nonselective NSAID pre-EGD discontinued NSAID use or had a PPI added to their regimen post-EGD. These results suggest that EGD findings had a direct effect on Rx fill patterns.

Rx Fills for PPIs and Nonselective NSAIDs Pre- and Post-EGD

	Pre-EGD (%)	Post-EGD (%)	Absolute Change (%)	Percentage Change (%)
EGD patients				
PPIs				
T2D (N = 39,636)	36.7	54.2	17.5*	47.7
Nondiabetic (N = 39,636)	35.9	53.0	17.1*	47.6
Nonselective NSAIDs				
T2D (N = 39,636)	7.6	6.2	-1.4*	-18.4
Nondiabetic (N = 39,636)	6.2	5.0	-1.2*	-19.4

\* $P < .0001$

883

#### Frequent Nighttime Symptoms and Increased GERD Symptom Severity Are Associated with Impaired Functioning

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**Purpose:** To assess health-related quality of life (HRQOL) among GERD patients stratified by symptom severity and by nighttime symptoms.

**Methods:** A sample of US adults participated in a web survey including a validated GERD screener. Frequency and severity of nighttime and daytime heartburn and acid regurgitation during the previous 3 months were each assessed. The highest value reported for symptoms during the daytime or nighttime was assigned to assess severity (10-point Likert scale). Severity classification was: mild (1–4), moderate (5–7) and severe (8–10). Nighttime GERD (NTG) cases were defined as: (a) symptoms  $\geq 2$  nights/wk with or without daytime symptoms, or (b) cases without daytime symptoms but at least one night/wk with symptoms. SF-36 Mental Component Summary (MCS) and Physical Component Summary (PCS) scores were calculated and mean scores were compared for NTG vs Daytime GERD (DTG) (t-tests), and by severity (ANOVA). Lower scores signify worse HRQOL.

**Results:** 2,805 of 18,213 invited to participate responded. 2,603 (mean age = 46 years, 55% women) satisfied the study criteria. Among 668 cases with current GERD symptoms, 303 had NTG and 365 had DTG; 664 cases had severity data: 155 were mild, 341 moderate, and 168 severe. GERD cases with NTG had lower MCS and PCS scores compared with DTG cases (Table 1;  $P < 0.05$ ). Among individuals with GERD, as GERD severity increased, MCS and PCS scores significantly decreased (Table 2;  $P < 0.05$ ). Differences between moderate and severe groups were twice as large as differences between mild and moderate groups.

**Conclusion:** HRQOL is significantly worse in patients with nighttime GERD symptoms. Symptom severity is also associated with decreased HRQOL. These findings suggest that even partial improvement in symptom severity or reduction in nighttime symptoms may lead to improved mental and physical functioning among symptomatic GERD patients.

Table 1. Mean MCS and PCS Scores for NTG vs DTG

	NTG (N = 303)	DTG (N = 365)
MCS	40.8	43.2
PCS	41.6	43.5

Table 2. Mean MCS and PCS Scores by GERD Severity

	Mild (N = 155)	Moderate (N = 341)	Severe (N = 168)
MCS	44.6	42.8	38.2
PCS	44.8	43.4	39.0

884

#### The Relationship between Atypical GERD Manifestations and Sleep Impairment

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**Purpose:** To assess sleep impairment among GERD patients experiencing frequent nighttime atypical manifestations of GERD.

**Methods:** A sample of US adults participated in a web survey including a validated GERD screener. Frequency of nighttime atypical GERD manifestations during the previous 3 months was assessed. Frequent symptoms were defined as atypical manifestations  $\geq 2$  nights per week for each manifestation. Sleep impairment during the previous 3 months was assessed using a five-category ordinal scale. The proportion with sleep impairment (ie, those reporting sleeping poorly often or most of the time) was compared for GERD cases with versus those without each nighttime atypical manifestation using the chi-square adjusting for multiple comparisons.

**Results:** 2,805 of 18,213 invited to participate responded. 2,603 satisfied the study criteria (mean age = 46 years, 55% women); 701 were GERD cases. Overall, 74% of GERD cases reported at least one nighttime atypical manifestation. For almost every daytime and nighttime atypical manifestation assessed, more than 20% of GERD patients reported their occurrence as frequent ( $\geq 2$  days or nights per week). For 8 of the 9 nighttime atypical manifestations assessed, the proportion of GERD cases reporting sleep

Percent with Sleep Impairment for GERD cases with vs without frequent atypical manifestations

	Infrequent or no manifestation	Frequent manifestation	P-value
	% with sleep impairment		
Fullness in Throat	35.5	62.1	<.0001
Sinusitis	35.1	51.7	.0001
Coughing	35.7	54.2	<.0001
Throat Clearing	33.7	53.2	<.0001
Sore Throat	37.0	59.2	<.0001
Snoring	39.9	44.6	NS
Wheezing	37.9	56.7	<.0005
Choking	39.1	63.1	<.0004
Non-cardiac Chest Pain	35.8	62.2	<.0001

impairment was significantly higher for GERD cases with the atypical manifestation compared with GERD cases without the atypical manifestation.

**Conclusion:** Most atypical GERD manifestations affected quality of sleep as perceived by individuals with GERD. Awareness of this relationship may assist in the management of these patients.

## 885

### Prevalence of Sleep Impairment among Adults with GERD

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**Purpose:** To identify and characterize possible sleep impairment among patients with GERD.

**Methods:** A general population of US adults participated in a web-based survey including the GERD Symptom & Medication Questionnaire, a validated GERD screening tool to determine GERD status. Nighttime GERD (NTG) cases were defined as: (a) symptoms  $\geq 2$  nights/week with or without daytime symptoms, or (b) individuals without daytime symptoms but at least one night/week with symptoms. Daytime GERD (DTG) cases were GERD cases not satisfying NTG criteria. Respondents not meeting the above criterion served as controls. Sleep impairment was compared for GERD cases versus controls and for NTG versus DTG during the previous 3 months using the chi-square test for trend.

**Results:** 2,805 of 18,213 invited to participate responded. 2,603 satisfied the study criteria (mean age = 46 years, 55% women); 701 were GERD cases. Among symptomatic GERD cases (N = 668); 303 met NTG criteria and 365 met DTG criteria. GERD cases had a higher prevalence of sleep impairment than controls (41.9% vs 19.4%;  $P < 0.0001$ ) (Table 1). NTG cases reported significantly more sleep impairment than DTG cases (49.5% vs 36.7%;  $P = 0.0003$ ) (Table 2).

**Conclusion:** GERD in general, and especially NTG symptoms, is associated with significant sleep disruption. Awareness of nighttime reflux and associated sleep complaints should allow more complete evaluation and treatment of GERD patients.

Distribution of sleep impairment by GERD vs Controls

	GERD (N = 701)	Controls (N = 1902)
Sleep impairment	% distribution	
Slept well almost all of the time	9.8	23.8
Slept well most of the time	19.3	30.8
Occasionally had trouble sleeping	29.0	26.1
Often had trouble sleeping	26.1	12.9
Slept poorly most of the time	15.8	6.5

$P < 0.0001$  for chi square test of distribution

Distribution of sleep impairment by NTG vs DTG

	NTG (N = 303)	DTG (N = 365)
Sleep impairment	% distribution	
Slept well almost all of the time	6.0	11.5
Slept well most of the time	17.8	20.0
Occasionally had trouble sleeping	26.7	31.8
Often had trouble sleeping	29.7	23.8
Slept poorly most of the time	19.8	12.9

$P = 0.0003$  for chi square test of distribution

## 886

### Exploratory Study Examining the Risk of Gastrointestinal Bleeding for Patients on Selective Serotonin Reuptake Inhibitor Therapy

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**Purpose:** Selective Serotonin Reuptake Inhibitors (SSRIs) are highly used in the treatment of depression; however their use has been associated with bleeding. There is current debate in the literature whether SSRIs are associated with gastrointestinal bleeding (GIB). This exploratory, retrospective claims-based analysis aimed to compare the incidence of GIB in patients continuously using SSRIs for at least 6 months compared with age and sex matched controls and examine factors that may be associated with the risk of GIB among SSRI users.

**Methods:** The MarketScan database (2001–2005) was used to identify patients  $\geq 18$  years, newly initiated on SSRI therapy. Inclusion criteria: continuous enrollment in the 12 months before and after the first SSRI prescription (index claim); consecutive SSRI use without a gap of  $>31$  days between prescriptions for at least 6 months. Exclusion criteria: received an SSRI prescription or had a GIB diagnoses within 1 year before the index claim. Logistic regression examined impact of age, gender, exposure (days supply of filled prescriptions) of SSRI, NSAID, gastrotoxic agents (GTAs; warfarin, corticosteroids, antiplatelets and calcium channel blockers), and gastroprotective agents (GPAs; proton pump inhibitors, histamine2-receptor antagonists) on odds of GIB.

**Results:** Sample had 149,647 SSRI users that met the inclusion criteria; mean SSRI exposure in follow-up period was 358 days (SD 79). SSRI incidence of GIB was 8.3/1000, compared to 6.4/1000 in controls. Percent use of NSAID, GTA, and GPA in SSRI patients ranged from 24–36% in the pre or post period. Mean days (across all patients) of NSAID, GTA, and GPA exposure was 39, 63, and 53 in the pre-period, and 48, 89, and 75 days in the follow-up period. Compared to 18–34 year old SSRI users, those 65+ years were 12 times(x) more likely to have GIB, rates were 6 $\times$  and 3 $\times$  higher for those aged 55–64 and 45–54. Female SSRI users were 1.4 $\times$  more likely to have GIB compared to males. GTA users were 2% more likely to have GIB for each additional 30 days of exposure (pre-period or follow-up period).

**Conclusion:** New SSRI users were 1.3 $\times$  more likely than controls to experience GIB. Among SSRI patients, older age, females, and use of GTAs were associated with having GIB. Additional research will investigate time to onset of GIB, and the influence of GIB events on subsequent SSRI, GTA, NSAID, and GPA use in the SSRI population.

## 887

### Impact of Sleep Difficulties on Economic and Humanistic Outcomes in GERD/Heartburn Sufferers

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**Purpose:** To study the association of GERD/heartburn (HB) and timing of its symptoms with sleep difficulties and the impact of sleep difficulties on health-related quality of life (HRQOL) and resource use in GERD/HB sufferers.

**Methods:** Data were from the 2006 US National Health and Wellness Survey, a nationally representative, Internet-based survey of the health status, attitudes, behaviors, and outcomes of adults. Those reporting GERD/HB in the past 12 months (N = 21,250) were compared with non-sufferers (N = 41,583) on 3 sleep difficulties outcomes: induction (difficulty falling asleep), maintenance (difficulty staying asleep/waking too early), and sleep-related difficulties (self-report of insomnia, sleep difficulties, induction or maintenance) for 2+ times a week. Among GERD/HB sufferers, those with GERD/HB problems during the day only (DO)[13.3%], at night only (NO)[28.2%], or during both day and night (DAN)[58.5%] were compared. Regression models were used to determine the independent effects of GERD/HB and its

timing on sleep difficulties and the impact of sleep difficulties on resource use and HRQOL, assessed by SF-8.

**Results:** GERD/HB sufferers were significantly ( $P < 0.001$ ) more likely to experience sleep-related difficulties (73 v 56%), induction (47 v 32%) and maintenance (63 v 46%) than non-sufferers. Controlling for demographics and comorbidities, GERD/HB sufferers were more likely to experience sleep-related difficulties (OR = 1.54, 95% CI = 1.48–1.60), induction (OR = 1.41, CI = 1.36–1.47), and maintenance (OR = 1.45, CI = 1.40–1.50) than non-sufferers. GERD/HB sufferers with sleep difficulties had significantly lower SF-8 physical and mental summary scores and reported more ER visits, days hospitalized, and provider visits in the past 6 months than those without sleep difficulties. A greater proportion of DAN sufferers experienced sleep-related difficulties (77 v 66 v 70%), induction (52 v 38 v 42%) and maintenance (67 v 55 v 59%) than DO or NO sufferers ( $P < 0.001$ ). Controlling for demographics, comorbidities, and GERD/HB treatment, DAN sufferers were more likely to experience sleep-related difficulties (OR = 1.43, CI = 1.30–1.57), induction (OR = 1.45, CI = 1.32–1.58), and maintenance (OR = 1.44, CI = 1.32–1.57) compared to DO sufferers.

**Conclusion:** Those with GERD/HB, chiefly DAN sufferers, are more likely than non-sufferers to experience sleep difficulties, mainly maintenance. The study provides quantitative evidence about the negative impact of sleep difficulties on resource use and HRQOL in GERD/HB sufferers.

## 888

### Utility of Screening Coagulation Studies in Gastrointestinal Bleeding Patients without Risk Factors for Coagulopathy Admitted to the Intensive Care Unit

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**Purpose:** Measurement of prothrombin time (PT), international normalization ratio (INR) and partial thromboplastin time (PTT) for patients admitted to the ICU with gastrointestinal bleeding (GIB) is routinely done regardless of risk factors for bleeding. This is a retrospective study to determine the percentage of abnormal PT/PTT/INR requiring correction prior to endoscopy in a cohort without risk factors for bleeding, and to evaluate if abnormal values are independent risk factors for rebleeding, hospital mortality, prolonged ICU and hospital stay.

**Methods:** Retrospective chart review of 300 consecutive admissions from the ED to the ICU for gastrointestinal bleeding. A total of 175 patients were identified as not having risk factors for bleeding disorders (defined as alcohol abuse, liver disease, and active use of anticoagulants). These patients were divided into normal (INR ≤ 1) and abnormal (INR > 1) cohorts. The percentage of patients requiring correction of coagulopathy was calculated. Also, length of stay in the ICU, total days in the hospital, rebleeding, and hospital mortality among the cohorts were compared.

**Results:** Five (5) of 175 admissions (3%) without risk factors for bleeding disorders underwent correction of their INR with fresh frozen plasma at time of admission. Cause of abnormal INR in all patients was attributed to malnutrition. Seventy-three patients had normal INR, and 102 had abnormal INR on admission. These two cohorts did not differ significantly in age, gender, and comorbidities as measured by the Charlson Comorbidity Index. There was no statistically significant difference in hospital mortality, inhouse rebleeding, and total days in the hospital between the two groups. The cohort with abnormal INR had a statistically significant longer length of stay in the ICU (3.6 vs 2.7 days,  $P = 0.002$ ).

**Conclusion:** It is uncommon for GIB patients without risk factors for bleeding disorders to present with abnormal coagulation tests that require correction. Abnormal INR is an independent risk factor for prolonged stay in the ICU by our observation. Prospective trials are needed to validate these findings.

## 889

### Is Obesity the Cause of Reduced Healing Rates in Advanced Grades of Erosive Esophagitis (EE)?

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**Purpose:** Obesity increases the transgastric pressure gradient and thereby predisposes to acid reflux. To determine whether BMI affects healing of different grades of EE in patients treated with proton pump inhibitors (PPIs).

**Methods:** This was a pooled analysis of 5 randomized, double-blind, multicenter clinical studies of similar design that compared esomeprazole 40 mg once daily to either omeprazole 20 mg once daily (SH-QBE-0013, -0016, and -0052) or lansoprazole 30 mg once daily (D9612C00083 and D9612L00046). Eligible patients were aged 18 to 75 y and had EE verified within 1 week of randomization by endoscopy and graded using the Los Angeles (LA) classification system. Endoscopy was repeated at 4 and 8 weeks to assess healing of EE, defined as no esophageal erosions. Healing rates were combined for all PPIs, assessed according to baseline LA grade (A, B, C, or D), and grouped according to BMI category. Logistic regression models (LRMs) were fit with healing of EE at the end of the study as the dependent variable and BMI as a continuous independent variable. The LRM adjusted for treatment, study, baseline LA grade, age, sex, race, *H. pylori* result, and presence of hiatal hernia. A second LRM was also fit to test for interaction of BMI with the other factors. A  $\chi^2$  test was performed to test for differences in the percentage of patients in each BMI category with severe (LA grade C or D) EE.

**Results:** This analysis included 11,027 patients. Healing rates at 8 weeks were comparable among the BMI categories (Table). The LRMs showed no significant effect of BMI on healing:  $P = .2286$ ; odds ratio, 1.006 (95% CI, 0.996–1.016). However, baseline LA grade was significantly ( $P < .0001$ ) associated with healing, with decreased odds of healing for higher LA grades. No interaction effects with BMI were found.

**Conclusion:** BMI had no detectable effect on healing of EE in patients treated with PPIs. Lower rates of healing after 8 weeks of treatment in patients with high grades of EE are not likely due to obesity.

Healing rates by BMI and baseline LA grade categories

Baseline EE	BMI Group	N	Healing Rate (%)
A	< 25	785	89.0
	25 to < 35	2,186	91.4
	≥ 35	506	91.5
B	< 25	635	83.5
	25 to < 35	2,629	86.9
	≥ 35	683	85.4
C	< 25	278	81.7
	25 to < 35	1,944	79.5
	≥ 35	437	78.7
D	< 25	107	72.9
	25 to < 35	614	70.4
	≥ 35	123	71.5

## 890

### Impact of Steroid Discontinuation on Health Care Resource Utilization in Crohn's Disease

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**Purpose:** Steroid use (SU) is associated with considerable morbidity, therefore the economic impact of SU in Crohn's disease (CD) could be important.

Steroids could also be surrogates for disease severity. This study determined whether discontinuation of SU among patients (pts) with CD lowers CD-related health care costs.

**Methods:** 9,811 pts with CD-related SU were selected from an Integrated Health Care Information Services (IHCIS) managed-care database (1999–2005). Index date is the first date of CD-related SU (CD within the past 30 days) after 3-month continuous insurance coverage eligibility. Pts with SU 60–90 days after the index date were steroid maintainers (SM). All others were steroid discontinuers (S-). Health care costs (total and CD-related) of S- and SM were evaluated over 3 months and compared descriptively. The same groups were then controlled for baseline (BL) characteristics (demographics, comorbidities, BL CD-related and non-CD related costs) using a regression-adjusted (Reg-Adj) model and compared. Costs were inflation-adjusted to year 2005 in US dollars (\$).

**Results:** Of the 9,811 CD pts selected, 5,614 were S- and 4,197 were SM. Mean age was 43.1 years for both groups, with 44.4% (S-) and 46.7% (SM) males. Both groups had similar prior total and CD-related costs. In the follow-up period, both total and CD-related costs were statistically significantly lower for S- when compared with SM (both  $P < 0.01$ ) (table). Total and CD-related Red-Adj costs were statistically significantly lower for S- when compared with SM (both  $P < 0.01$ ). Significantly lower CD-related costs were observed for all components of S-, including inpatient, outpatient, and prescription drug costs.

3-Month Health Care Costs by Steroid-Use Status

	Descriptive Costs, US \$		Reg-Adj Costs, US \$	
	Total	CD-related	Total	CD-related
SM (N = 4,197)	10,786	5,270	9,513	5,352
S- (N = 5,614)	7,759*	3,275*	8,477*	3,209*

\* $P < 0.01$ , S- vs. SM for respective cost groups.

**Conclusion:** Significant total costs were observed for patients with continuous steroid use. Steroid discontinuation was significantly associated with lower total and CD-related health care costs. These results demonstrate that continuous steroid use may have significant cost implications for society and third-party payers. Therapies that help patients taper off steroids may yield cost savings.

## 891

### Gender Differences and Bariatric Surgery Outcome

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**Purpose:** Bariatric surgery is an effective treatment for obesity, however it does not lead to equal results in every patient. Although the prevalence of obesity in women in the US parallels the increase in men, little data exists on differences in predictors of bariatric surgery outcome between men and women. The aim of this study was to identify gender differences in predictors of weight loss success in the first year after bariatric surgery.

**Methods:** The charts of all patients who underwent laparoscopic adjustable gastric banding (LAGB) or Roux-en Y gastric bypass (RYGB) between 10/1/2000 and 10/31/2005 were reviewed. Demographic data, social history, past psychiatric history, personal and family history of obesity, self and professionally assessed eating behavior, as well as post-op data on excess body weight loss at 1, 3, 6 and 12 months follow-up were collected for each patient. Post-op weight loss success was defined as  $> 50\%$  of excess weight loss (EWL) at 12 months.

**Results:** A total of 1,722 patients were evaluated and 635 without follow-up data at 12 months were excluded. Among the 1,087 analyzed individuals, 994 (88%) had the LAGB and 136 (12%) had RYGB. Women made up 73% and 83% of patients in the LAGB and RYGB groups respectively. The mean age was  $41 \pm 12$  y and  $44 \pm 12$  y for women and men respectively. The racial distribution was similar in both groups. The initial mean BMI was  $44.8 \text{ kg/m}^2$  and  $47.7 \text{ kg/m}^2$  for women and men. 70% of men were married, compared to only 48% of women ( $P < 0.001$ ). Women had a higher number of negative pre-op social psychiatric factors compared to men ( $7.4 \pm 3$  vs.  $6.3 \pm 3$ ,  $P < 0.001$ ), but were more likely to achieve successful EWL compared to their male counterparts (53% vs. 38%,  $P < 0.001$ ). Factors that were predictive of successful EWL among women included late night eating ( $P = 0.018$ ), not eating carbohydrates ( $P = 0.020$ ), being socially avoidant ( $P = 0.029$ ), and having a marriage that was impacted by obesity ( $P = 0.016$ ). None of these factors were predictive of post-op weight loss success in men.

**Conclusion:** In this cohort we identified significant gender differences in bariatric surgery outcome as well as in the predictors of successful post-op weight loss. Further evaluation is warranted to better understand the impact of these factors on long-term weight loss outcome.

## 892

### Are Proton-Pump Inhibitors (PPIs) Associated with an Increased Risk of Community-Acquired Pneumonia (CAP)? A Nested Case-Control Study Investigating Recent PPI Exposure and CAP

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**Purpose:** Limited data suggest that proton-pump inhibitor use may increase the risk of developing community-acquired pneumonia. We aim to further assess the effect of recent PPI use on the risk of developing CAP in a large, population-based cohort.

**Methods:** We conducted a nested case-control study in the General Practice Research Database (GPRD) (1987–2003). The GPRD is a computerized medical record system from the United Kingdom containing complete, prospectively-collected prescription data. The study cohort included all patients aged  $\geq 18$  years and with  $\geq 6$  months of pneumonia free follow-up in the GPRD. Cases included all patients with an incident CAP diagnosis. Up to 10 controls were selected for each case using incidence density sampling, matching on practice site, calendar period, and duration of follow-up prior to the index date. The primary exposure was the presence or absence of any PPI prescription in the 30 days prior to the index date. In a secondary analysis, we compared the effect of once daily versus twice daily PPI dosing. Adjusted odds ratios (AORs) were estimated using conditional logistic regression adjusting for age, sex, measures of healthcare utilization, alcohol use, smoking, BMI, a comprehensive list of co-morbid conditions, and medications that may alter immune status or compromise CNS or oropharyngeal function. Effect modification was also examined for patients  $\geq 65$  versus  $< 65$  years of age.

**Results:** When adjusted for sex and age, the OR for CAP associated with recent PPI use was 1.8 (95% CI 1.7–1.9). After adjusting for all additional confounders, recent PPI exposure showed a minimally increased risk of CAP (AOR 1.1 95% CI 1.0–1.2). This small increase in risk was limited to patients  $< 65$  years old (AOR 1.3 95% CI 1.2–1.5), while patients  $\geq 65$  years old were at no increased risk (AOR 1.0 95% CI 0.9–1.1). Twice daily PPI dosing was also associated with a higher risk of CAP (AOR 1.3 95% CI 1.1–1.6) than once daily dosing (AOR 1.1 95% CI 1.0–1.1).

**Conclusion:** Recent PPI use was associated with an increased risk of developing CAP after adjusting for sex and age. However, after adjusting for multiple measured confounders, the increased risk of CAP was minimal. This increased risk was primarily seen with twice daily dosing and younger PPI users.

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### Coffee Grounds Emesis: Always an Underlying Gastrointestinal Bleeding Problem?

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**Purpose:** Acute GI blood loss manifests as hematemesis, melena and/or hematochezia. Initial management is identical irrespective of nasogastric (NG) aspirate results. Current practice includes early upper endoscopy. Significantly fewer high-risk bleeding lesions are found on endoscopy in patients with coffee grounds vs. bloody NG aspirates GIE 2004;59:172–78.

We present a case series to illustrate that patients with coffee grounds emesis (CGE) and coffee grounds NG aspirate often have other unsuspected medical illnesses that may be overlooked by pre-occupation with the GI bleed.

**Methods:** Retrospective chart review of six patients presenting with CGE who were admitted for the upper GI bleeding.

**Results:** All patients were hemodynamically stable at admission.

NG lavage showed coffee grounds that cleared easily.

None of the patients rebled or required blood transfusions during their hospital stay.

See table 1 for demographics, associated illness, endoscopic findings and outcome.

Pt.1: Referred for endoscopy which was deferred, pt. deemed unstable from new onset atrial fibrillation. Acute myocardial infarction ruled in.

Pt.2: Constipation at presentation overlooked and diagnosis of small bowel obstruction delayed by work-up of CGE.

Pt.3: Diagnosis of urosepsis made after septic shock developed 12 hours after admission.

Pt.4: Admitted for CGE. Extensive pulmonary emboli found subsequently on evaluation of dyspnea which was present on admission.

Pts.5 and 6: Admitted to ICU because of large volume of CGE despite no drop in BP and Hb/Hct. Pt.5 had acute renal failure.

**Conclusion:** Priority with work-up of GI bleeding including endoscopy delayed the diagnosis of serious, even life threatening illnesses. Hemodynamically stable patients who present with coffee grounds NG aspirate and no fall in Hb/Hct should be evaluated for other associated non-GI bleeding conditions.

Patient	Age	Sex/ Race	Associated Disease	Endoscopy	Outcome
1	70	M/W	Myocardial Infarction	not done	discharged
2	55	M/W	Small Bowel Obstruction	Gastric Erosions	discharged after surgery
3	82	M/W	Urosepsis	not done	recovered with antibiotics
4	89	F/W	Pulmonary Emboli	not done	discharged after recieving IVC filter
5	63	F/W	Acute Renal Failure	normal	resolved with hydration
6	60	M/W	no major illness	normal	discharged after endoscopy

894

### Comparison of Resource Consumption in GERD Care by Primary Care Providers and Gastroenterologists

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**Purpose:** Driven by our hypothesis that the medical approach to gastroesophageal reflux disease (GERD) and (&) resource consumption differ for primary care providers (PCPs: general practitioners, internists) & gastroenterologists (GEs), the purpose of this study is to define, quantify & compare resource consumption for patients (pts) with GERD treated by PCPs and GEs.

**Methods:** Retrospective medical & pharmacy claims data from a national health plan with 14 M lives. Pts with  $\geq 2$  GERD-related diagnoses (ICD9 530.1x, 530.2x, 530.3, 530.81, 530.85, 787.1) or medications (proton pump inhibitors (PPIs), H2 receptor agonists (H2RAs), or other (sucralfate, bethanechol, metoclopramide)) were identified from 11/1/01–10/31/04 & observed for  $\geq 1$  year. Episode Treatment Group software created episodes (eps) of integrated comprehensive GERD-related care in defined timeframes. Eps were labeled PCP or GE if  $\geq 55\%$  of claims in eps were associated with PCP or GE, respectively. Procedures, prescriptions (rx) & sequences of PCP & GE care were measured.

**Results:** Sample included 270,325 pts with 54% female & mean age 46( $\pm 14$ ) years. There were 228,719 PCP eps & 46,241 GE eps. Among all PCP & GE eps, pts had mean 0.8( $\pm 0.4$ ) eps/year with mean episode length of 5.4 months. PPIs alone were the main drug therapy; 70% & 68% of all PCP & GE eps, respectively, had rx for PPIs only. The 2nd most common rx was H2RA for PCPs (9% eps) versus GEs, who added other rx to PPI (5%). Pts were sent to GEs during PCP eps (PCP-GE referral (ref)); after PCP eps (PCP-GE transfer); or before PCP eps (GE-PCP transfer). PCP-GE ref eps and GE eps were more likely to have physician visits & endoscopies versus non-PCP-GE ref eps; all chi-square significant at  $P < 0.01$ .

	GERD Care Resource Consumption					
	PCP-GE Referral		PCP-GE Transfer		GE-PCP Transfer	
	No GE Ref	GE Ref	PCP Ep	GE Ep	GE Ep	PCP Ep
# (%) all pts	5,521 (2%)		1,859 (0.7%)		1,874 (0.7%)	
# eps	220,051	8,668	2,100	2,265	2,189	2,247
% eps with physician visit	54%	85%	64%	82%	78%	51%
% eps with endoscopy	2%	60%	2%	37%	31%	3%

Eps with GE care were more likely ( $P < 0.01$ ) to have esophagoplasty, fundoplasty, other tests (e.g., Bernstein) although  $<4\%$  eps had those procedures (data not shown).

**Conclusion:** Pts transferred or referred to GEs had relatively high resource consumption via physician visits & endoscopies. Pts transferred to PCPs after GE eps appeared to use fewer GERD-related visits versus pts who went to PCPs before GEs.

895

### Infliximab Persistence: Treatment of Crohn's Disease from a Payor Perspective

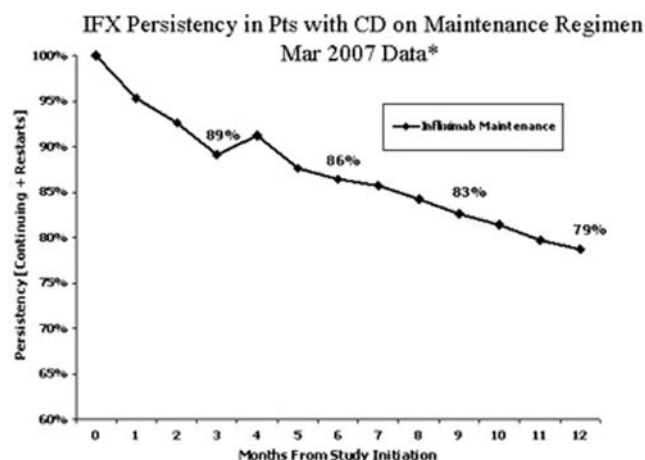
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**Purpose:** To evaluate the persistence of infliximab (IFX) maintenance therapy for the treatment of patients (pts) with Crohn's disease (CD) utilizing the Wolters Kluwer (WK) and PharMetrics claims databases.

**Methods:** Longitudinal claims data from PharMetrics and WK were analyzed. Pts enrolled in the same plan for 12 mos after the initial claim were evaluated. The first IFX treatment (index date) among pts with CD in the

period Dec 1 2003 – Feb 28 2004 was identified. Only pts in the PharMetrics database who were eligible for continuous coverage for at least 12 mos following the initial claim were evaluated. Pts were included in the maintenance regimen group only if their first 2 infusions were within the study period and were between 5–10 wks apart, or if the first 2 infusions were <5 wks apart and the third infusion was 5–10 wks after the second. A cohort was developed based on the first IFX treatment date. IFX persistence (%) was defined as the % of pts in the cohort that either had an IFX claim in the calendar month 12 mos after the index date, or had a claim within 56 days prior to the calendar month 12 mos after the index date. Beginning with the Feb 2004 cohort, PharMetrics-derived persistency rates were updated based on a trend analysis of WK claims data for index dates of Feb 2004, Mar & Sep 2005, and Mar 2006.

**Results:** 891 pts receiving IFX were analyzed. In the Feb 2004 cohort, the IFX persistence rates decreased over a 12 mo time period from 89% at 3 mos, 80% at 6 mos, and to 73% at 12 mos; 95% CI (70–76%). Based on a trend analysis of WK data cohorts initiating on Feb 2004, Mar 2005, Sep 2005, and Mar 2006, IFX persistence appears to be similar, and is estimated at 89% at 3 mos, 86% at 6 mos, and at 79% at 12 mos; 95% CI (76–82%). After the third month of treatment, IFX persistence was over 88% (79%/89%) for the duration of the yr. [figure1]



**Conclusion:** IFX persistence in pts with CD is high ( $> 73\%$  in both) over a 12-month time period in analyses conducted on 2 databases. Moreover, persistence was much higher after the first three mos of therapy ( $> 88\%$ ).

## 896

### Development and Validation of the pH-Metry Impact Scale (pHIS) and pH-Metry Symptoms Scale (pHSS)

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**Purpose:** Ambulatory wireless pH-metry has gained popularity because of improved patient tolerability and decrease restrictions on normal diet and activity. Few studies have quantified patient's experiences during wireless or catheter-based pH-metry and no validated questionnaires exist for the quantification of the impact of pH-metry on daily activities or symptoms. Primary aim was to develop and validate the pHIS and pHSS to assess patient's changes in activities of daily living and symptoms during pH-metry.

**Methods:** The pHIS included seventeen items selected by literature review and expert consensus to reflect the impact of pH-metry on activities of daily living. Item responses were coded on a 7-point Likert-type scale anchored with 'none of the time' to 'all of the time'. The survey was administered to out-patients undergoing pH-metry. Principal Component Analysis (PCA)

with Varimax rotation and Kaiser Normalization (SPSS v15) was completed. Internal consistency was assessed according to Cronbach's alpha. The pHSS quantified pH-metry associated changes in 12 symptoms by their frequency, severity and bothersomeness on 5-point Likert-type scales. Non-parametric Mann Whitney tests were used for preliminary comparisons.

**Results:** Sixty seven consecutive patients (51 F;  $59 \pm 16$  yrs and 16 M;  $64 \pm 11$  yrs) undergoing wireless ( $N = 51$ ) or catheter-based pH-metry ( $N = 16$ ) completed the pHIS and pHSS. PCA of the pHIS suggested a 3-component solution that accounted for 72% of total variance: "Social-Emotional Impact" (46%), "Impact on Daily Activities" (16%), and "Dietary Impact" (10%). Cronbach's alphas ranged from 0.86–0.92, supporting good internal consistency. Wireless pH-metry patients experience less melancholy when compared to catheter-based ( $0.49$  vs  $1.19$ ,  $P < 0.01$ ), were less likely to be socially impacted ( $P < 0.01$ ) and more likely to continue daily activities ( $0.61$  vs  $1.56$ ,  $P < 0.05$ ). Foreign body sensation in chest was increased in wireless patients ( $1.60$  vs  $.25$ ,  $P < 0.01$ ), whereas foreign body throat was more frequent in catheter patients;  $2.94$  vs  $1.02$   $P < 0.01$ .

**Conclusion:** The pHIS and the pHSS demonstrated good psychometric properties and can provide a validated instrument for assessment of the impact on activities of daily living and patient's symptoms during pH-metry. Assessing changes in daily activities and symptoms during pH studies may improve clinical interpretation of these diagnostic tests.

## 897

### Can the Occurrence of Septic Complications after Restorative Proctocolectomy Be Predicted?

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**Purpose:** To evaluate preoperative and operative factors that might be associated with the development of septic complications after restorative proctocolectomy (RP).

**Methods:** From a prospectively maintained pouch database, patients developing abdominal and pelvic septic complications after RP were identified. The association of patient, disease and technical factors and the development of septic complications was determined. Complication rates within subgroups were analyzed with Kaplan-Meier analyses, and comparisons performed using log rank tests.  $P < 0.05$  was considered to be significant.

**Results:** There were 3215 patients (56.1% male) in the database. Final pathologic diagnosis was inflammatory bowel disease 92%, FAP 6%, cancer 0.8%, dysplasia 0.4%, and others 0.8%. 84.2% underwent diversion proximal to pouch. 251 (7.8%) patients who developed septic complications were identified. There was no association between septic complications and age ( $P = 0.9$ ), gender ( $P = 0.3$ ), primary indication ( $P = 0.06$ ), presence of anal findings (0.22), prior colectomy (0.08), pouch anastomosis type (0.06) or proximal diversion ( $P = 0.47$ ). Comorbidity ( $P < 0.05$ ), hypoalbuminemia ( $P < 0.01$ ), final pathological diagnosis ( $P < 0.001$ ) and intra-operative transfusion ( $P < 0.01$ ) were significantly associated with the development of septic complications. Perioperative immunosuppressant use ( $P < 0.001$ ) was significantly associated with the development of septic complications. Amongst the patients on immunosuppression, Remicade ( $P < 0.01$ ) and Imuran use ( $P < 0.05$ ) was significantly associated with sepsis in contrast to steroid use ( $P = 0.2$ ), which was not associated with sepsis.

**Conclusion:** Patients treated perioperatively with Remicade and Imuran, and those with associated comorbidity, hypoalbuminemia, and requiring intraoperative transfusion are more likely to develop septic complications after RP.

## 898

### Systemic Antibiotic Prophylaxis for Percutaneous Endoscopic Gastrostomy: A Meta-Analysis



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**Purpose:** Percutaneous endoscopic gastrostomy (PEG) tube placement is associated with a risk of infection. Despite numerous guidelines recommending prophylactic antibiotics prior to PEG tube placement, their use remains controversial. We performed a meta-analysis to establish whether prophylactic use of systemic antimicrobials reduces the risk of peristomal and systemic infection in patients undergoing placement of PEG tubes.

**Methods:** MEDLINE (1966–2007), PubMed, Cochrane Central Register of Controlled Trials & Database of Systematic Reviews, and abstracts from gastroenterology scientific meetings (last 5 years) were searched (June 2007). Only randomized controlled trials (RCTs) of adult subjects comparing prophylactic antibiotic to no prophylactic antibiotic for PEG tube placement were included. Study quality was assessed by assigning a quality score. Two independent reviewers used standard forms to extract data and the differences were resolved by mutual agreement. Meta-analysis for the effects of prophylactic antibiotic was analyzed by calculating pooled odds ratio for peristomal infections, systemic infections, and mortality using both fixed and random effects models. Heterogeneity among studies was assessed by calculating I measure of inconsistency. Publication bias was assessed by constructing funnel plots.

**Results:** Ten RCTs (N = 1,051) met the inclusion criteria. Five trials used cephalosporins, 3 trials used penicillin, and 2 trials used either penicillin or cephalosporins. Prophylactic antibiotic with PEG tube placement resulted in a significant reduction in the incidence of peristomal infection (OR 0.42, 95% CI: 0.30–0.59,  $P < 0.01$ ) and systemic infection (OR 0.22, 95% CI: 0.13–0.39,  $P < 0.01$ ). No significant difference was noted for mortality (OR 0.67, 95% CI: 0.35–1.26,  $P = 0.21$ ). Heterogeneity among studies was not significant. Funnel plots revealed no significant publication bias. All studies received a high score for quality.

**Conclusion:** Administration of prophylactic antibiotic prior to PEG tube placement is effective in reducing the incidence of peristomal infections and systemic infection.

## 899

### Missed Cancers vs Procedure-Related Complications: Balancing the Medico-Legal Risks of Surveillance Colonoscopy

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**Purpose:** Data suggest that gastroenterologists perform surveillance colonoscopy more often than recommended by guidelines. This practice may be driven by medico-legal concerns over missed cancers. Though more frequent colonoscopy may reduce the risk of missed cancers, it also increases the risk of procedure-related complications. According to malpractice data, such complications, particularly colonic perforation, are the most common reason for litigation against gastroenterologists. Yet, no study has compared the frequency of missed cancers and colonic perforations in patients undergoing “intensive” vs recommended colonoscopic surveillance.

**Methods:** We developed a Markov model to determine the number of opportunities for litigation in a cohort of 1000 men/women  $\geq 50$  yrs of age with a new diagnosis of colon adenomas. We modeled 2 surveillance strategies: (1) an “intensive” strategy with colonoscopy every 3 years in all patients; and, (2) a “recommended” strategy with colonoscopy every 3–5 yrs based on current guidelines. The base-case assumptions (and ranges for sensitivity analysis) were: (1) risk of colonic perforation: 0.25% (0.1%–0.4%); (2) relative risk of litigation due to missed cancer vs perforation: 1.0 (1.0–3.0); and, (3) advanced adenoma miss rate: 6% (0%–12%).

**Results:** In the base-case analysis, the “intensive” strategy resulted in 46 opportunities for litigation over the lifetime of the cohort (22 perforations & 24 missed cancers). In contrast, the “recommended” strategy endorsed by current guidelines resulted in only 40 opportunities for litigation (14

perforations & 26 missed cancers). In sensitivity analysis, the number of opportunities for litigation under the “intensive” strategy was greater than under the “recommended” strategy even when the perforation rate was reduced (0.1%), when the relative risk of litigation due to an interval cancer was increased (3-fold), or when the advanced adenoma miss rate was increased (12%).

**Conclusion:** Compared to the recommended strategy, more intensive surveillance is associated with slightly fewer missed cancers but substantially more colonic perforations, resulting in more opportunities for litigation. This result was robust to a wide range of assumptions in sensitivity analysis. Endoscopists who disregard current guidelines and perform more intensive surveillance out of concern for missed neoplasia should carefully weigh the competing risk of procedure-related complications.

## 900

### Knowledge of Hepatocellular Carcinoma (HCC) Screening Guidelines and Current Practices: Results of a National Survey

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**Purpose:** HCC is the fifth most common cancer in the world. The AASLD recommends HCC screening for high risk patients. Previous survey studies have demonstrated that many gastroenterologists either do not know or disregard guideline recommendations about colon polyp surveillance even when they do understand them. However, no prior studies have evaluated practicing gastroenterologists’ knowledge of HCC screening recommendations, including management of positive screening tests.

**Methods:** A 12-item multiple choice survey about HCC screening was developed based on 2006 AASLD guidelines. Content validation was performed with expert review. For each question, respondents reviewed a clinical scenario, identified the appropriate intervention based upon guideline recommendation, stated if they were certain about guideline recommendation for this question, and identified their usual practice. The survey was distributed to physicians attending two major GI certification and recertification examination review courses (Mayo Clinic GI Board Review and William Steinberg Board Review in GI).

**Results:** 42% (224/537) of potential respondents completed the survey. 71% (160/224) were attending physicians with median age of 41 yrs and median practice of 11.5 yrs. 8% had never heard of HCC guidelines. 97% correctly identified that AFP alone or alternating with ultrasound was inappropriate for HCC screening. 94% used ultrasonography for HCC screening. 85% of respondents correctly identified the high risk patients for HCC screening, however, only 33% knew the appropriate age to start HCC screening among female Asian chronic hepatitis B carriers. 30% did not know that the guideline recommendation for  $\geq 2$  cm hypervascular lesion suspicious for HCC was referral for liver transplantation. Among those who knew guidelines, virtually 100% self-reported that they followed the guidelines in their own practices.

**Conclusion:** The majority of physicians correctly identified the common high risk scenarios, methods and duration of HCC screening. However, 30% of gastroenterologists did not know that Child B cirrhotic patient with  $\geq 2$  cm lesion suspicious for HCC should be referred for liver transplantation. As opposed to previous data on colon polyp surveillance, gastroenterologists appear to know most HCC screening guidelines and apply most of these recommendations in their own practice.

## 901

### Cost-Effectiveness of Lubiprostone in a Managed Care Population with Chronic Idiopathic Constipation

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**Purpose:** Treatment of chronic idiopathic constipation (CIC) can be costly. Recently, medications used to treat CIC over longer time periods have been approved and have been consistently reimbursed. Understanding the economic consequences of these treatments as currently prescribed in managed care health plans is important to decision-makers. To assess cost effectiveness of treating patients with lubiprostone from a United States (US) healthcare payer perspective.

**Methods:** We developed a Markov model to compare treatment with lubiprostone to tegaserod in adult patients with history of CIC (per Rome II Guidelines). Perspective of the third party payor was modeled. Age and gender distributions of CIC patients were taken from an analysis of managed care claims data. Treatment patterns were applied as observed in managed care claims data which included treatment with tegaserod in patients over 65 years of age. Treatment efficacy data, rescue medication use, and symptoms scores were extracted from FDA Approved Clinical Trials and product labels. Direct cost data were drawn from standard US costing sources (WAC prices) and published analyses of claims data. The model was projected over a one-year time horizon.

**Results:** Among CIC patients prescribed lubiprostone or tegaserod within a managed care health plan, those treated with lubiprostone had lower drug costs (\$1,547 versus \$1,746) and fewer medical costs (\$2,330 versus \$2,486) than patients on tegaserod. Patients on lubiprostone had more symptom-free days than patients on tegaserod (326 versus 301, respectively). Fewer lubiprostone-treated patients required rescue medications than those on tegaserod (35.3% versus 47.1%, respectively). As a result, treating with lubiprostone was dominant compared to tegaserod. In probabilistic sensitivity analyses, 91.4% of 1000 simulations demonstrated dominant results.

**Conclusion:** Based on analyses of managed care treatment patterns, lubiprostone is less costly and more effective than tegaserod for treatment of CIC. Cost-effective options for reimbursement remain available.

## 902

### Healthcare Utilization and Cost in Pediatric Gastroesophageal Reflux Disease (GERD) Patients on Continuous vs. Intermittent Proton Pump Inhibitor (PPI) Treatment Regimens

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**Purpose:** To compare healthcare utilization and costs in two distinct PPI treatment regimen groups in the pediatric GERD population: continuously treated with PPIs vs. intermittently treated with PPIs.

**Methods:** Patients were identified from a privately insured claims database (1999–2005) using the following criteria: age < 18 years at date of first PPI prescription (index) and one GERD diagnosis (ICD-9-CM: 530.11, 530.81, 787.1) in the 6-month period before the index. A 1-year washout period was used to ensure that no other PPIs had been used prior to index date. The continuous group (CG) was identified as patients having a PPI episode longer than 30 days starting at index. The intermittent group (IG) was identified as patients having a first PPI episode of 30 days or less followed by a discontinuation of 30 days or more, and then another PPI episode. Healthcare utilization rates and costs were measured for the 1-year period prior to index date (baseline) and 1-year post index date (follow-up), and compared between the two regimens using Student and Wilcoxon tests. Patients concomitantly using PPIs and H2 Receptor Antagonists during either the baseline or follow-up period were excluded.

**Results:** The samples included 1,026 continuous and 310 intermittent PPI users. CG and IG patients had similar demographic and comorbid characteristics at baseline. The mean length of treatment for CG group during follow-up was 170 days (median = 120 days). On average, IG patients had 2.1 episodes (median = 2 episodes), and were off treatment for 104 days (median = 91 days). CG patients experienced an average reduction of \$4,351 in total cost (medical + pharmacy) in the follow-up compared to baseline,

while IG patients experienced an average increase of \$686 in total cost (difference \$5,037,  $P = 0.009$ ). The CG patients also experienced a reduction by 0.11 GERD-related inpatient stays compared to a 0.06 increase for the IG patients ( $P = 0.006$ ).

**Conclusion:** The results suggest that pediatric GERD patients who are continuously treated with PPI experience a relatively larger benefit in terms of total cost savings than do patients treated intermittently. Further studies are needed to assess the impact of different age and risk groups on these cost savings.

## 903

### Use and Abuse of Proton Pump Inhibitors

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**Purpose:** To determine the utilization of proton pump inhibitors (PPIs) at an academic medical center we evaluated the indications for PPI use in hospitalized patients, and the frequency in which patients placed on a PPI during hospitalization were discharged on a PPI.

**Methods:** We performed a prospective analysis of 502 consecutive patients admitted at the Medical College of Georgia (MCG) and the Children's Medical Center (CMC) who received a PPI. Patients who were on a PPI at home and not placed on one at the time of admission were not accounted for in this study. We recorded demographics, indication for use, hospital service prescribing PPI, route of administration, PPI use prior to admission, and discharge PPI medication for each admission.

**Results:** Between May 6th and June 19th, 2005, a total of 2,497 patients were admitted to MCG and CMC. 502 were prescribed a PPI. Analysis of the adult population revealed 463 (26%) patients admitted to MCG were prescribed a PPI. Patients received a PPI for the following indications: stress ulcer prophylaxis (SUP)-53%, GERD-30%, not documented -15%, GI bleed-5%, continuation of home medication-4%, other-4%, esophagitis-0.1%, and peptic ulcer disease-0.1%. 37% of patients were on a PPI prior to admission. Although 246 patients (53%) were placed on a PPI for prophylactic purposes, only 18% were admitted to the intensive care unit. Overall, 300 of the 463 patients (~65%) were prescribed a PPI without a documented appropriate indication. Upon discharge, 50% of patients were prescribed a PPI. 22% of patients placed on a PPI for prophylactic purposes were discharged on a PPI. Overall, about 55% of patients were discharged on a PPI without appropriate indication or documentation.

**Conclusion:** There is significant overuse of PPIs in the inpatient setting at our institution with about 26% of patients receiving a PPI on admission, and 55% of patients discharged on a PPI without any clear indication or documentation. Caution must be used when initiating PPI therapy in the hospital setting; long-term therapy often continues unnecessarily after discharge leading to increased healthcare costs, polypharmacy, and increased risk for potential adverse effects including *Clostridium difficile* diarrhea, community-acquired pneumonia, and intestinal bacterial overgrowth. Therefore, physicians need to be aware of the indications and possible consequences of PPI use in hospitalized patients.

## 904

### Comparison of Lactose Versus Lactulose Breath Tests in Subjects Suspected with Small Intestinal Bacterial Overgrowth

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**Purpose:** Evidence for comparative utility of various carbohydrate substrates in hydrogen breath testing (HBT) for the diagnosis of small intestinal bacterial overgrowth (SIBO) is scant. The aim of this study was to compare the yields for lactulose vs. lactose HBT in suspected SIBO. We determined: 1) the frequency of SIBO; 2) the level of rise in hydrogen (H) & methane

(CH3); & 3) the time to rise in H or CH3 with the highest sensitivity for SIBO with each carbohydrate substrate.

**Methods:** All subjects who underwent HBT from 2003–06 at Rush University Medical Center were identified using the HBT database, cross referenced to a billing database. Subjects were excluded if they had HIV, immunosuppression, antibiotic use, widespread malignancy or terminal illness. For HBT, 25 gm of lactose or 20 gm of lactulose were used. Two baseline samples & samples every 15 mins were taken up to 165 mins and analyzed using the Quinton Microlyzer for H, CH3 & carbon dioxide (CO<sub>2</sub>). The clinical data & the HBT results were obtained via chart review and were analyzed with chi-square, Fisher exact tests for categorical data, & Kruskal-Wallis tests for continuous variables, using SPSS v. 11.5 & S+7.0. HBT were considered positive for SIBO if there was a double peak in H or CH3 in lactose or lactulose HBT; or the hydrogen level was > 20 ppm before 90 min in lactulose HBT. The tests were read by a single experienced gastroenterologist.

**Results:** Patient related variables such as age, gender, pre- or post-test symptoms or diagnosis, past medical or surgical history, medications, endoscopic or histological findings from EGD &/or colonoscopy, hemoglobin & albumin did not differ significantly between the patients receiving lactose HBT (N = 110) vs. lactulose HBT (N = 85). There was no statistically significant difference in the frequency of SIBO in subjects who underwent lactose (36.7%) versus lactulose (40%) HBT ( $P = 0.221$ ). There was no statistically significant difference between mean CH3 levels at any time interval with either substrate, although there was a trend towards higher CH3 levels at all time intervals in lactulose HBT. Mean CH3 levels in lactose vs lactulose peaked at 30 mins vs 60 mins, respectively in those with SIBO.

**Conclusion:** Lactose and lactulose HBT yield similar results in SIBO diagnosis. Use of the lactose substrate could be considered in those patients suspected to have lactose intolerance and SIBO.

## 905

### Differences in Health Care Visits Coded for Potential Proxy Conditions/Symptoms of Gastroesophageal Reflux Disease (GERD) before and after a GERD Diagnosis: A Pediatric Database Study

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**Purpose:** To examine changes in frequency of medical visits coded for potential proxy conditions and/or symptoms of GERD (PPCSG) before and after a GERD diagnoses in a large pediatric claims database.

**Methods:** All children aged 2–18 years coded for a GERD diagnosis (ICD-9-CM: 530.10–12, 530.81, 787.1) twice within a six month period in the MarketScan®<sup>1</sup> claims database (2001–2005) and continuously in the database for 6-month before (pre) and after (post) the first GERD diagnosis (index) were included. One control patient, matched by gender, birth year and state of residence, was identified for each GERD patient, assigned the index date of the matched GERD patient, and confirmed to be retained in the database continuously for 6-month pre and post index date. Experts in the field generated a list of ICD-9 codes representing PPCSG. For each PPCSG, the mean number of visits coded for each PPCSG were compared for the pre and post periods.

**Results:** The sample included 17,123 GERD patients and their 17,123 controls. For most of the selected conditions, no significant changes were found in the mean number of visits pre and post index for the control sample ( $P > 0.05$ ). For the GERD sample, significant reductions in the mean number of visits were identified for several selected conditions: acute sinusitis ( $P < 0.01$ ), cough ( $P = 0.04$ ), croup ( $P < .01$ ), otitis ( $P < .01$ ), and pneumonia ( $P < .01$ ). Significant increases were found in several others: abdominal pain ( $P < .01$ ), chest pain ( $P < .01$ ), nausea/vomiting ( $P < .01$ ), and unspecified anorexia ( $P < .01$ ).

**Conclusion:** The results show that visits for many PPCSG which are potential extraesophageal manifestations of GERD decreased after a GERD diagnosis, suggesting the possibility that recognition and treatment of GERD resulted in improvement of outcomes of these conditions. Potential PPCSG with increases in visit numbers after the GERD index were generally more typical gastrointestinal GERD symptoms. Further study is required to understand this finding. <sup>1</sup><http://www.medstatmarketscan.com>. Accessed on June 11, 2007.

## 906

### The Economics of Gastrointestinal Bleeding in US Managed Care

#### Setting: 12-Month Costs and Outcomes

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**Purpose:** Gastrointestinal (GI) bleeds require intensive medical intervention and could lead to escalated health resource utilization (HRU) over the patient's lifetime. This study estimates the incremental cost of GI bleeding and associated outcomes compared to a control cohort over a 12-month follow-up.

**Methods:** US national health-plan claims data (1999–2004) were used to identify patients hospitalized with an upper GI bleeding event. These patients were propensity matched to control patients from 10% sample taken from the same US health plan, without evidence of GI bleeding, based on a nearest neighbor matching method. The propensity score model included age, gender, date of index date (quarter/year), Charlson Comorbidity Index, geographic region, and prior medical utilization. Expenditures are the sum of health plan and patient paid amounts.

**Results:** 8,823 GI bleed patients and 579,018 control patients meeting inclusion criteria were identified. Propensity score matching yield 7,646 matched pairs. Mean age was 53 in both cohorts and 50.2% of patients with GI bleed were male compared to 56% in the control group. Charlson comorbidity index was 0.54 and 0.48 respectively, for the GI bleed patients and controls. Among the GI bleed patients, total health care expenditure averaged \$24,036 in the year following hospital admission compared to the annual average of \$5,111 per person in the general population ( $P < 0.001$ ). Main cost drivers for the GI bleed cohort were inpatient hospitalizations while outpatient visits and prescription pharmacy accounted for 23% of expenditures (Table 1). Risk of re-hospitalization among GI bleed patients was 24%. Patients with GI bleed had on average, an additional 0.7 ER and 4.5 outpatient visits compared to controls ( $P < .001$ ).

**Conclusion:** 12-month HRU for patients experiencing GI bleed was significantly higher than that of controls without GI bleed. Additional research is necessary to document GI bleed recurrence over a longer timeframe.

**Table 1.** Annual Health Care Expenditures.

	GI Bleed	General Population	P-value
Total	\$24,036	\$5,111	<0.001
Medical	\$21,769	\$3,303	<0.001
Inpatient	\$14,844	\$1,090	<0.001
Outpatient	\$3,270	\$1,374	<0.001
ER	\$411	\$103	<0.001
Other Medical	\$3,244	\$736	<0.001
Pharmacy	\$2,267	\$1,808	<0.001

## 907

### Medical, Pharmacy, and Sick Leave Costs for Constipation and for Irritable Bowel Syndrome with Constipation in the 6 Months before and after Diagnosis: An Employer Perspective

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**Purpose:** Both constipation (C) and irritable bowel syndrome with C (IBS+C) are known to be very costly. However, whether the costs of C are driven by the same factors that drive IBS+C costs is unknown. We aimed to assess the cost of illness (COI) for C without and with IBS (IBS+C) among US-based employees.

**Methods:** A retrospective analysis was conducted using the Human Capital Management Services Research database, which represents multiple US-based employers and contains employee health claims data from 2001–2005. Data included medical, pharmacy, payroll, work absence, and demographics. ICD9 Codes were used to include employees in the C cohort: 564.0 (Constipation), 564.00 (Unspecified), 564.01 (Slow Transit), and 564.09 (Other). Employees with C and an ICD9 for IBS (564.1×) at any time were included in the IBS+C cohort. Propensity scores based on demographics, job-related variables, region, existence of medical claims, and Charlson Comorbidity Index Score were used to match 5 C employees to each IBS+C cohort employee. For the C cohort the index date was the date of the first C claim. For the IBS+C cohort the index date was the date of the first IBS claim. Mean costs for each cohort were adjusted to 2006\$ and compared by category for medical, prescription drug (Rx), and sick leave costs in the 6-months before and after index diagnosis (dx).

**Results:** Data were available for 1854 employees. Demographics for both cohorts were similar ( $P > .05$ ). All between cohort COI comparisons (Figure) were similar ( $P > .05$ ), except for Rx costs after dx (\$26 higher for IBS+C,  $P = .036$ ). Within cohort comparisons (6-months before vs. after dx) identified significant increases in medical and Rx costs for both cohorts ( $P \leq .05$ ). Sick leave costs and days increased after dx in both C and IBS+C cohorts ( $P > .05$ ). Persons with IBS+C averaged an additional 1.3 sick leave days during the 6-month period after dx when compared with the C cohort ( $P < .03$ ).

**Conclusion:** Costs of illness for IBS+C and C are very similar. Total costs and sick leave days for both cohorts increased after dx.[figure1]

Cost Category	Time (relative to DX)	Per-member-per-month			
		Constipation		IBS+C	
		N	Mean Cost (\$)	N	Mean Cost (\$)
Medical	Before	1,545	450	309	499
	After		689 <sup>#</sup>		623 <sup>#</sup>
Prescription Drug	Before		88		98
	After		107 <sup>#</sup>		134 <sup>#</sup>
Sick Leave	Before	751	68	157	86
	After		73		106
Total	Before		606		683
	After		869		862

\* Between cohorts  $P = .0363$

# Within cohort (Before vs. After)  $P \leq .05$

## 908

### Infliximab Therapy for Patients with Crohn's Disease: Analysis of Health Care Utilization

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**Purpose:** We sought to evaluate the relationship between infliximab and subsequent health resource use and costs in privately insured patients with Crohn's disease (CD) using observational data from the 1999–2003 Medstat MarketScan commercial claims and encounters databases.

**Methods:** We undertook a 12-month pre-post (before and after infliximab), and 2-year prospective risk adjusted case-control analysis of integrated inpatient, outpatient, and prescription drug claims. Three-hundred and ninety-six, and 7,938 plan participants older than 18 years of age with a diagnosis of CD were included in the pre-post, and case-control analysis, respectively.

**Results:** We found no differences in mean number of admissions (0.49 versus 0.51 admissions;  $P = 0.79$ ) or length of hospitalizations (2.6 versus 3.3 days;  $P = 0.16$ ), or in mean number of emergency department [ED] visits (0.62 versus 0.65 visits;  $P = 0.74$ ) during the 12-month periods before and after infliximab, respectively. Increases were seen in mean number of outpatient visits ( $\Delta = +2.4$  visits;  $P < 0.001$ ) and mean number of prescription drug fillings ( $\Delta = +5.1$  fillings;  $P < 0.001$ ) when counts of events were compared 12-months after infliximab to counts before infliximab ( $\Delta = \text{post minus pre}$ ). Infliximab therapy was associated with a mean increase of \$15,524 in total 12-month expenditures ( $P < 0.001$ ). In the 2-year prospective case-mix adjusted models, with a propensity score covariate to account for disease severity, no significant differences in rates of hospitalization (rate ratio [RR] of 0.82;  $P = 0.183$ ) or ED visits (RR of 1.05;  $P = 0.550$ ) were seen. Infliximab was associated with a higher rate of outpatient office visits (RR of 1.54;  $P < 0.001$ ). Case-mix adjusted mean total expenditures during the 2-year follow-up period were higher for infliximab users than for those who did not receive infliximab (\$40,686 versus \$22,109, respectively;  $P < 0.001$ ).

**Conclusion:** Taken together, the results of the pre-post and case-mix adjusted analyses suggest that infliximab therapy is not associated with an overall reduction in direct healthcare resource utilization when used in actual practice by privately insured patients with CD.

## 909

### Effect of a Liver Psychology Team on Mental Health Related Treatment Discontinuation Rates

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**Purpose:** Hepatitis C (HCV) has a higher prevalence in veterans. Despite availability of effective therapies, unacceptably high therapy (tx) discontinuation rates remain a significant barrier to successful outcomes with combination tx. Veterans have increased mental health co-morbidities and decreased rate of tx candidacy, as well as premature discontinuation of HCV tx secondary to mental health side-effects. The overall discontinuation rates in registration trials were reported to be 13–15%. Mental health related discontinuation rates as high as 15% have been reported with IFN based treatments. The effect of a liver psychology team on treatment discontinuation rates is not well established.

**Methods:** A database was created to evaluate the interaction of hepatitis C and diabetes. Out of this database 148 patients were identified to have received tx for hepatitis C between 1999 and 2006. We evaluated the mental health tx discontinuation rates in this very diverse group of patients, including post-transplant, pre-transplant, re-treatment and tx naïve patients.

**Results:** From 1999–2006 148 patients were identified in the database that were treated with interferon based therapies. Mean age was  $53.0 \pm 0.5$ . 98% were male. 64 patients (43%) completed therapy. 52 (35.1%) were discontinued for non-response. 32 (21.6%) were discontinued prematurely secondary to side-effects. Of the 32 patients, who discontinued tx for side effects, 7 (21.9%) had mental health reasons. Overall 4.3% of the patients were discontinued for mental health reasons. 17.9% of patients seen by liver

psychology had MH discontinuations as opposed to 50% of the patients not seen by liver psychology. 7 out of 96 patients treated prior to 2003 as opposed to 0 out of 45 patients treated after 2003 had treatment discontinuation for MH reasons.

**Conclusion:** Mental health co-morbidities leading to decreased therapy candidacy and treatment discontinuations represent a significant barrier to therapy. An integrated liver psychology team can have a significant impact on therapy discontinuation rates.

## 910

### Gastrointestinal Bleeding in Biopsy-Proven Graft-Versus-Host Disease of the GI Tract: Risk Factors and Effect on Mortality

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**Purpose:** Graft-versus-host disease (GVHD) is the leading cause of morbidity and mortality after allogeneic bone marrow transplantation. Gastrointestinal tract (GIT) involvement presents with diarrhea, abdominal pain, vomiting, and upper or lower GI bleeding. Risk factors for GI bleeding and its effect on mortality have not been described. The purpose of this study is to identify the risk factors for GI bleeding in GVHD and determine its effect on survival.

**Methods:** We reviewed the medical records of patients with biopsy-proven GVHD of the GIT after allogeneic hematopoietic stem cell transplantation (HSCT) from 1/2000 to 12/2006 at our institution.

The patients were grouped into those with no evidence of GI bleeding, patients with mild bleeding (< 6 units of PRBC's transfused) and patients with severe bleeding (> 6 units).

**Results:** We identified 73 of 489 patients (15%) with HSCT and biopsy-proven GVHD of the GIT; 39 patients (53%) were male. Nineteen patients (26%) had severe GI bleeding, 4 (5%) had mild bleeding and 50 (68%) had no bleeding.

Mean age for patients with severe bleeding was 41 years compared to 42 years in patients with no bleeding. 73% of patients (14/19) with severe bleeding were male compared to 46% of patients (23/50) with no bleeding ( $P = 0.039$ ).

There was a trend toward more endoscopic finding of erosions, ulcers, necrosis or bleeding in patients with severe bleeding, 73%, compared to 50% of patients with no bleeding ( $n = 25$ ,  $P = 0.076$ ).

Of the patients with severe GI bleeding, 95% ( $n = 18$ ) had clinical grade 3 or 4 GVHD compared to 48% of patients with no bleeding ( $n = 24$ ) ( $P = 0.0003$ ). 79% of patients with severe bleeding ( $n = 15$ ) had histological grade 3 or 4 compared to 58% of patient with no bleeding ( $n = 29$ ,  $P = 0.001$ ).

The average onset of GIT GVHD symptoms after HSCT was 8 days earlier in patient with severe bleeding (26 vs. 34,  $P = 0.46$ ).

The overall 6 month-mortality rate in patients with severe bleeding was 79% ( $n = 15$ ) compared to 54% ( $n = 27$ ) in patients with no bleeding ( $P = 0.096$ ).

**Conclusion:** Our data suggest that male gender, clinical grade of 3 or 4, and histological grade 3 or 4 were associated with the development of GI bleeding in GVHD of the GIT. Patient age and onset of symptoms showed no correlation with increased risk of bleeding. Endoscopic findings, however, seemed to suggest more risk of bleeding.

There was a trend toward increase in overall 6 month-mortality rate after HSCT in patients with severe GI bleeding.

## 911

### Patients Discharged from a Chest Pain Center – Are They Followed up and Treated Appropriately?

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**Purpose:** Chest pain (CP) centers represent an important advance in the diagnosis and rapid treatment of patients presenting with chest pain of cardiac ischemic origin, as patients undergo a structured protocol to rapidly identify and treat acute cardiac ischemic injury. What happens to patients discharged from the chest pain unit with acute ischemic injury having been “ruled out” is the subject of this report.

**Methods:** We were able to contact 44 consecutive patients, ages 36 to 84 (mean age 61) discharged from our CP center 30 to 60 days previously. They were asked to consent to a phone interview. 39 of 44 agreed to participate. We described symptoms that would likely relate their CP to a gastrointestinal origin (heartburn, dysphagia, upper abdominal pain, regurgitation, nausea or vomiting) and inquired whether these symptoms were present. We determined whether physician follow-up was obtained. We inquired whether diagnostic tests had been performed, whether GI consult had been obtained, and whether presenting symptoms were still present at the time of our interview.

**Results:** 33 of the 39 patients had followed up with their primary care provider (PCP). 23 of 39 had concurrent symptoms strongly suggestive of a gastrointestinal origin of CP and had discussed this with their PCP. Only 2 had been referred to a Gastroenterologist. Additionally, 22 of the 39 continued to have the symptom that prompted their visit to the CP Center.

**Conclusion:** GI symptoms (and, hence, likely CP origin) are common in patients discharged from a CP center. While most patients had medical follow up with their PCP, diagnostic tests were rarely performed, and, in the majority of patients, symptoms persisted. As a result of this information, we have initiated a protocol whereby all patients discharged from the CP center will have structured follow up with a GI consultant, contact being established with an “on call” Gastroenterologist prior to their discharge from the chest pain unit.

## 912

### Prospective Assessment of Electronic Health Record (EHR) Implementation on Community Based GI Practice

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**Purpose:** EHRs are increasingly utilized in GI practices with the promise of increased practice efficiency, improved safety, and decreased cost. There is limited data on the ability of EHRs to achieve these intended endpoints. This abstract compares the impact of EHR implementation on two community based GI practices.

**Methods:** Huron Gastro (HG) is an 18 provider practice in Michigan that installed the NextGen EHR in 2004 and was fully implemented in 2006. The Center for Digestive and Liver Health (CDLH) is a 15 provider practice in Georgia that implemented the Allscripts EHR in 2005. Clinical outcomes and costs pre and post implementation were assessed.

**Results:** Prior to implementation, the average time for a referring doctor to receive a dictated consultation was 14 days (range 7–28 days). Post implementation, this time decreased to hours after completion of the consultation at both practices. HG medical records FTE preimplementation was 1 per 3 providers, post implementation 1 per 4 providers. CDLH medical records FTE preimplementation was 5 per 6 providers, post implementation 3 per 8 providers. HG annualized pre-implementation transcription costs were 112K compared to 12K post implementation. CDLH annualized pre-implementation transcription costs were 71K compared to 29K post implementation. HG postage costs decreased from \$20K to \$6.5 during the same comparative period. When the drug Zelnorm was withdrawn from the market due to safety concerns, all patients using Zelnorm at both practices were identified within 24 hours and contacted by mail or phone to discontinue the drug. Similar efforts to identify patients when Cisapride was withdrawn took over a week in 2000 at HG.

**Conclusion:** Community based GI practice EHR implementation resulted in reduction in the time for referring physician to receive consultation notes

by an average of 2 weeks at both practices, decreased medical record FTEs, decreased transcription costs, and decreased postage costs. These findings suggest EHR implementation improves the efficiency of communication and decreases practice costs. Allowing easy database searches to identify patients at risk for drug toxicity may enhance patient safety. The cost savings achieved by EHRs are countered by the significant cost associated with implementation and the hiring of dedicated IT staff.

## 913

### Frequency and Indications for Performance of Repeat Colonoscopy within Sixty Days

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**Purpose:** Overuse of colonoscopy affects the availability, quality, and cost of care. We sought to evaluate the frequency and indications for repeat colonoscopy within 60 days, and to evaluate whether baseline patient characteristics or the course during the first colonoscopy predicted the need for repeat procedures.

**Methods:** We identified 781 patients who had more than one colonoscopy within 60 days, among 51559 patients (1.5%) who underwent colonoscopy during Jan 2004 to Dec 2006. Control patients who did not have repeat exams were matched with the study population with respect to procedure date and location. Medical records were reviewed for patient demographic and historical data and numerous procedural characteristics. Univariate and multivariate logistic regressions were performed to assess the association between the repeat colonoscopy and patient age, gender, BMI, history of abdominal surgery, procedure tolerance, size of largest polyp, endoscopist experience, inpatient vs. outpatient status, and use of anticoagulants, narcotics or benzodiazepines.

**Results:** The most common reasons for repeat colonoscopy included poor bowel preparation (32%), "Need for Complex Therapy" (21%), bleeding management (13%), pathology follow-up (12%), stricture therapy (6%), failure due to intolerance (4%), failure due to anatomy (4%), and anticoagulant or antiplatelet agent mgmt (2%). Multivariate logistic regression showed statistically significant differences between the study and control populations in regard to age (OR = 1.01; 95% CI 1.003–1.017;  $P < 0.005$ ), history of abdominal surgery (OR = 1.68; 95% CI 1.34–2.11;  $P < 0.0001$ ), procedural tolerance level (OR = 4.01; 95% CI 2.20–7.30;  $P < 0.0001$ ), inpatient versus outpatient status (OR = 1.78; 95% CI 1.31–2.41;  $P < 0.001$ ), largest polyp size  $\geq 2$  cm (OR = 10.70; 95% CI 5.08–22.56;  $P < 0.0001$ ), and use of anticoagulants (OR = 1.58; 95% CI 1.12–2.22;  $P < 0.001$ ). Endoscopist experience, and patient gender, BMI, or use of narcotics or benzodiazepines did not correlate with repeat procedures.

**Conclusion:** Poor bowel preparation and referral for complex therapies are the dominant indications for repeating colonoscopy within 2 months. Variables associated with performance of repeat colonoscopy included older age, history of previous abdominal surgery, inpatient status, poor procedure tolerance, largest polyp size more than 2 cm, and use of anticoagulants at the time of the first colonoscopy.

## 914

### Impact of an Internet-Based Educational Program on Colonoscopy Attendance and Quality

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**Purpose:** Poor patient compliance with attendance for scheduled colonoscopies leads to inefficiencies in scheduling and potential delays in diagnosis. Patient education techniques such as pre-procedural visits and telephone reminders have been shown to improve attendance rates. Poor compliance with

the pre-procedural preparative regimen may lead to cancelled procedures or insufficient visualization of the colonic mucosa.

EMMI™ (Expectation Management and Medical Information; Emmi Solutions, Illinois) is an online program that allows patients to learn about colonoscopy and its preparation prior to their procedure. This study aims to measure its utility in improving attendance and preparation quality.

**Methods:** Consecutive English-speaking competent adult patients scheduled for an outpatient colonoscopy upon referral from the primary care group at our institution were assigned an EMMI number and instructions to access the system prior to their procedure. Computer workstations were available for patient use. The primary outcome was attendance at the scheduled colonoscopy date; secondary assessments included quality and impact of the preparative regimen, and timing and reasons for cancellations. Fisher-exact, Chi-square, T-test, ANOVA, and logistic regression tests were performed, where appropriate.

**Results:** 333 patients were assigned EMMI numbers (65% female, mean age 60, range 25–93 years). 45 patients (13.5%) viewed the program prior to colonoscopy, predicted by younger age (mean 57 vs. 61,  $P = 0.04$ ) but not gender. Watching EMMI was predictive of attending scheduled colonoscopy (89% vs. 68%,  $P = 0.005$ ; irrespective of gender or age in regression analysis). 16.9% of patients who attended their colonoscopy had watched EMMI as compared to 5.2% of non-attendees. Too few patients who watched EMMI subsequently cancelled their colonoscopy (5) to allow for comparison of cancellation times and reasons between the two groups. Cancellation due to poor preparation was more common in older patients (mean age 60 vs. 48,  $P = 0.208$ ), irrespective of gender or EMMI status. Quality of preparation and impact on cecal intubation rates were not predicted by gender, age, or EMMI status.

**Conclusion:** Patients who watched an Internet-based education program prior to their colonoscopies were more likely to attend their colonoscopies than non-viewers. In an increasingly technological society, Internet-based pre-procedural education programs may help improve procedure attendance and other outcomes.

## 915

### Primary Sclerosing Cholangitis Is a More Common Indication for Orthotopic Liver Transplantation among African American Than Non-African American Patients

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**Purpose:** Primary sclerosing cholangitis (PSC) is a progressive, incurable condition of unknown etiology, characterized by inflammation, fibrosis, destruction and loss of interlobular-sized bile ducts, leading to biliary cirrhosis and liver failure. Orthotopic liver transplantation (OLT) is the only life-extending intervention for patients with end-stage PSC. Recent US Scientific Registry of Transplant Recipients (SRTR) data indicate that among patients with PSC being added to the United Network for Organ Sharing (UNOS) waiting list the proportion of African Americans (AA) was greater than non-AAs, compared to other disease indications. This suggests that PSC may run a more aggressive clinical course. It was our aim to determine whether the proportion of AA patients with PSC undergoing OLT per unit time was different from the proportion of non-AA patients undergoing OLT for PSC.

**Methods:** The SRTR was reviewed between 1998 and 2002 inclusive for all adults (18–80 years) who were added to the UNOS waiting list for OLT. The proportions of AA and non-AA patients undergoing OLT for PSC within 1 year, 1–2 years, 2–3 years, and  $> 3$  years of being added to the waiting list were calculated, and compared using the Chi-square test.

**Results:** From 1998 to 2002 inclusive 39,878 patients were added to the UNOS waiting list for OLT. 2173 (5.45%) had PSC. Of these, 262 (12.1%) were AA. The proportions of AA patients with PSC who underwent OLT within 1 year, 1–2 years, 2–3 years, and  $> 3$  years of being added to the waiting list were: 28.2% (74/262), 13.7% (36/262), 8.8% (23/262) and 5.7% (15/262). 114/262 (43.5%) AA patients with PSC did not undergo OLT

during the study period. The proportions of non-AA patients with PSC who underwent OLT within 1 year, 1–2 years, 2–3 years, and > 3 years of being added to the waiting list were: 33.5% (640/1911), 11.5% (220/1911), 4.7% (89/1911) and 4.9% (93/1911). 869/1911 (45.5) non-AA patients with PSC did not undergo OLT during this period. Except for the period < 1 year from the time of OLT listing, the proportion of AA patients with PSC undergoing OLT was significantly greater than the proportion of non-AA patients with PSC who underwent OLT ( $P = 0.026$ ).

**Conclusion:** These outcomes for AA patients with PSC suggest that their disease course may be more aggressive, given that patients underwent OLT sooner from the time of listing than did non-AA patients. An alternative explanation is that AA patients with PSC were simply sicker than non-AA patients at the time of listing for OLT.

## 916

### Economic and Humanistic Outcomes Associated with Timing of GERD/Heartburn Symptoms

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**Purpose:** To study the impact of timing of GERD/heartburn (HB) symptoms on economic and humanistic outcomes, specifically health-related quality of life (HRQOL), work productivity/activity impairment, and resource use.

**Methods:** Data were from the 2006 US National Health and Wellness Survey, a nationally representative, Internet-based survey of the health status, attitudes, behaviors, and outcomes of adults. Among respondents who reported experiencing GERD/HB in the past 12 months, the GERD/HB symptoms were categorized as occurring during the day only (DO), at night only (NO), or during both day and night (DAN). The 3 groups were compared on: HRQOL assessed by SF-8, work/activity impairment measured by Work Productivity and Activity Impairment Questionnaire and resource use. Chi-square and ANOVA were used to test for significant differences among categorical and continuous variables, respectively. All comparisons were tested for significance at  $P < 0.001$  level.

**Results:** Of the 21,250 individuals who reported experiencing GERD/HB, 13.3% reported DO symptoms, 28.2% NO symptoms, and 58.5% DAN symptoms. DAN sufferers were significantly more likely to be female, younger, experienced more frequent and severe symptoms, and are more likely to use pharmacotherapy than DO or NO sufferers. DAN sufferers reported significantly lower physical and mental HRQOL (43.92, 45.38 respectively) than DO (47.15, 48.70) and NO (47.28, 48.08) sufferers. Among those employed full-time, DAN sufferers reported significantly greater percentage work productivity loss in the past 7 days compared to DO and NO sufferers (18.57 v 14.94 v 14.99%), with impairment while at work contributing more than absenteeism. DAN sufferers reported significantly greater activity impairment compared to DO and NO sufferers (37.12 v 27.40 v 27.01%). In the past six months, DAN sufferers reported significantly higher number of hospitalizations and physician visits (0.67, 6.35 respectively) than DO (0.44, 4.80) and NO sufferers (0.40, 4.60). Using linear regression models to control for demographics and comorbidities, the significant differences in HRQOL, work/activity impairment and resource use remained.

**Conclusion:** More than half of GERD/HB sufferers experience symptoms both during the day and night. Due to the worse HRQOL, higher resource utilization and greater work/activity impairment associated with DAN symptoms, GERD/HB sufferers with DAN symptoms may have a significant economic and humanistic impact on patients, employers and society.

## 917

### Does Abnormal Computed Tomography (CT) of the Gastrointestinal (GI) Tract Correlate with Endoscopic Findings?

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**Purpose:** To determine the clinical significance of incidental GI tract abnormalities identified on CT.

**Methods:** A single center retrospective study identified patients undergoing endoscopic evaluation for luminal GI tract abnormalities detected on CT. Patient selection utilized a search of the electronic medical record for ICD-9 code 793.4 (nonspecific abnormal findings of GI tract on radiology exam). Only patients with abnormal CT were included.

**Results:** 77 patients underwent endoscopy specifically for GI tract abnormalities noted on CT. The most common indication for the CT scan was abdominal pain. Contrast (oral and iv) was used in 66 patients. CT findings included thickened appearance of the bowel wall, mass lesions and stenoses. Subsequent endoscopic findings are:

#### Colonoscopy (43/77 patients)

Gender (M/F)	22/21
Age (years) (Avg $\pm$ SD)	56.65 $\pm$ 19.9
Abnormal findings	
a) Terminal ileum/ileocecal valve	5/9 (55.5%) (ileitis-4, malignancy-1)
b) Right colon (cecum/ascending/hepatic flexure)	4/12 (33.3%) (ischemia -1, colitis -1, adenoma-2)
c) Proximal left colon (splenic flexure/descending)	3/5 (60%) (malignancy-1, adenoma-2)
d) Rectosigmoid	10/17 (58.8%) (malignancy-3, adenoma-2, miscellaneous*-5)

(\*miscellaneous: proctitis-1, volvulus-1, colitis-2, stenosis-1)

#### Esophagogastroduodenoscopy (34/77 patients)

Gender (M/F)	13/21
Age (years) (Avg $\pm$ SD)	63 $\pm$ 12.8
Abnormal findings	
a) Distal esophagus	5/16 (31.2%) (hiatal hernia-3, fundoplication-1, varices-1)
b) Stomach (body)	3/8 (37.5%) (malignancy-1, adenoma-2)
c) Antrum	0/7 (0%)
d) Duodenum	2/3 (66.6%) (adenoma-1, granulation tissue-1)

**Conclusion:** Gastroenterologists routinely perform endoscopy to address abnormalities discovered on imaging. This study addresses our center's experience and found differences from previously published data which primarily identified correlation in the rectosigmoid and distal esophagus. In our study, the highest correlation between CT findings and endoscopic abnormalities occurred in the terminal ileum, proximal left colon, rectosigmoid area and duodenum. Although not all findings revealed sinister pathology, endoscopy remains the primary modality to investigate radiologic abnormalities of the GI tract.

## 918

### Single-Dose Crossover Pharmacokinetic/Pharmacodynamic Study of Fospropofol vs Propofol in Healthy Volunteers

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**Purpose:** Fospropofol disodium (FP, AQUAVAN®) is a water-soluble pro-drug of propofol being developed for sedation in adults undergoing diagnostic and therapeutic procedures. FP is rapidly and completely metabolized to propofol (P<sub>FP</sub>) *in vitro*. This study compared the PK/PD and safety profiles of FP versus propofol (P, DIPRIVAN®) in 12 healthy subjects (20–40 yr).

**Methods:** In this open-label, 2-period, crossover study, each subject received a 10 mg/kg IV bolus of FP in the 1st period. The resulting maximal EEG effect was recorded by minimal bispectral (BIS) index. Depth of sedation was scored using the Modified Observer's Assessment of Alertness/Sedation (MOAA/S) scale. After a 7-day washout, in the 2nd period subjects received a 50-mg/min infusion of P titrated to produce a similar EEG effect as with FP. For PK evaluation, venous plasma samples were obtained during both periods, predose and up to 4 h postdose. Samples were assayed for FP by LC/MS/MS and for both P<sub>FP</sub> and P by HPLC with fluorescence detection. BIS measurements were obtained at 1 min predose, 1 min postdose, and at 2-min intervals until 20 min postdose or until the subject became fully alert.

**Results: PK and PD parameters**[figure1]PK and PD parameters for P<sub>FP</sub> differed from P, displaying a longer onset and duration of response, consistent with the observed concentration-time profile of P<sub>FP</sub>. Mean  $t_{1/2}$  values for P were similar for both treatments. The most common treatment-emergent adverse events (AEs) after FP (paresthesias and pruritis) were mild and self-limited; the most common AE after P treatment was mild dizziness.

Parameter Mean (SD)	Fospropofol (n=12)		Diprivan (n=12)
Analyte	Fospropofol	Propofol	Propofol
$T_{max}$ (min)*	4.0 (1.0-6.0)	0.0 (0.0-13)	4.0 (4.0-8.0)
$C_{max}$ (µg/mL)	114 (17.5)	2.20 (0.432)	5.16 (2.76)
AUC <sub>0-∞</sub> (µg·h/mL)	27.1 (3.90)	3.07 (0.49)	1.72 (0.42)
$t_{1/2}$ (h)	0.84 (0.09)	2.09 (0.62)	1.99 (0.57)
Minimum BIS Score		54.0 (6.9)	57.7 (7.1)
Time to Minimum BIS Score (min)		8.2 (3.2)	4.7 (1.4)
Minimum MOAA/S Score		1.3 (1.1)	0
Time to Minimum MOAA/S Score (min)		7.2 (4.2)	4.2 (1.2)
Area above the BIS-time curve	769 (323)		592 (130)

$T_{max}$  = Time to  $C_{max}$ ;  $C_{max}$  = maximum plasma concentration; AUC<sub>0-∞</sub> = area under plasma concentration-time curve, time 0 to ∞;  $t_{1/2}$  = terminal-phase elimination half-life  
\* Median (range)

**Conclusion:** FP dosing was well-tolerated, with no serious AEs. FP displays distinct differences in PK and PD compared to P, including a longer time to peak effect and a greater duration of effect.

## 919

### Efficacy and Safety of Teduglutide in Parenteral Nutrition (PN)-Dependent SBS Subjects: Update of a Current Multinational Trial

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**Purpose:** Massive small intestinal resection creates malnutrition, diarrhea, and dehydration as a consequence of reduced intestinal capacity to absorb nutrients, and this can lead to dependence on parenteral nutrition (PN) therapy. Unfortunately use of PN is also associated with serious complications, however, it is vital for many short bowel syndrome (SBS) patients. Teduglutide, an analog of glucagon-like peptide-2 (GLP-2), is being evaluated for safety, tolerability, and efficacy in reducing PN dependency in SBS patients. We present the design and baseline characteristics of this multinational trial.

**Methods:** Eligibility criteria included: 18 years and older; SBS resulting from major intestinal resection; PN dependency for at least 12 months; PN required at least 3 times weekly; and preserved renal and hepatic function. Subjects then entered into an intensive stabilization period to optimize PN volume before being randomized to placebo or 0.05 or 0.1 mg/kg/day of

teduglutide for a 24-week treatment, with follow-up 4 weeks post-treatment. Reduction in PN usage at 24 weeks of therapy was the primary endpoint, calculated as an ordered categorical response. Additional assessments included plasma citrulline, 72-hour balance studies, villous height, crypt depth, bone density, and quality of life.

**Results:** A total of 139 subjects were screened and 84 randomized (37 male), with 13 withdrawing. Up to 71 patients are expected to complete the study. Forty percent of subjects were recruited from the US and Canada, 60% from the EU. Subjects developed SBS due to surgical resections for: CD (37%); vascular accidents (30%); trauma (11%); and volvulus (13%). Sixty seven percent of subjects had a colon in continuity and 35% had a stoma. The average remaining length of small bowel was 66 cm and 69 cm of colon. Of the 20% of subjects with a distal/terminal ileum, 53% had an ileocecal valve. The DSMB reviewed safety throughout the study and found no specific concerns.

**Conclusion:** The target of randomizing at least 80 PN-dependent SBS patients in the teduglutide study was achieved, making this the largest clinical trial to evaluate a treatment to decrease PN requirements in SBS patients. The ability to reduce PN by enhancing enteral function, the therapeutic goal of teduglutide, has the potential to lead to improved quality of life in the SBS population.

## 920

### Impact of Adalimumab (HUMIRA®) on Patient-Reported Outcomes

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**Purpose:** Adalimumab (ADA) is approved for the treatment of adults with moderate to severe Crohn's disease (CD). Limited research has been reported on the impact of anti-TNF therapy on depressive (D) and fatigue (F) symptoms.

**Methods:** To assess the effect of ADA maintenance on F and D symptoms and traditional patient-reported outcomes (PROs), among randomized responders (RR) [pts with  $\geq 70$  point decrease from baseline CDAI score at Week (Wk) 4] in CHARM. All pts received a starting regimen of open-label (OL) ADA: 80 mg at BL (Wk 0), 40 mg ADA at Wk 2. At Wk 4, pts were stratified by response and randomized to a maintenance regimen: 40 mg ADA EOW or EW, or PBO. Differences in PROs [SF-36, IBDQ, FACIT-Fatigue (F), and Zung Depression scale (ZD)] at Wks 0, 4, 12, 26, and 56 were evaluated for those receiving ADA induction only (IO) and ADA maintenance (IM) therapy among RR. Fatigue was measured by FACIT-F (scale range 0–52), a 3–4 point change was considered clinically meaningful. Depressive symptoms were measured by ZD (scale range 20–80, with  $> 50 = D$  state).

**Results:** 499 responders were randomized at Wk 4 (IO, N = 170; IM, N = 329). Week 0 PROs indicated impaired health-related quality of life (HRQOL). The mean Wk 0 FACIT-F score = 23, similar to cancer pts with anemia. The mean Wk 0 ZD score (IO = 55, IM = 56) suggested depression among CD pts. Pts improved across all 4 PROs during the IO phase (Wk 4 vs. Wk 0). PROs from Wks 12–56 showed significantly improved HRQOL for pts in the IM group vs. the IO group. FACIT-F scores showed F symptoms were reduced in the IM group ( $P < 0.01$  vs. IO). Reductions in ZD scores showed statistically significantly reduced D symptoms in the IM group ( $P < 0.01$  vs. IO). SF-36 Physical Component (PCS) and Mental Component (MCS) Summary PROs were greater for the IM group at Wks 26 and 56 (all  $P \leq 0.05$  vs. IO). Disease-specific IBDQ score improvements were highly significant and sustained for the IM group ( $P < 0.01$  vs. IO) throughout the study.

**Conclusion:** Substantial and sustained benefits were observed for fatigue and depression outcomes in CD patients receiving ADA maintenance therapy. Adalimumab maintenance therapy also resulted in significant and sustained improvements in CD-specific (IBDQ) and general (SF-36, PCS and MCS) HRQOL measurements, compared with induction only therapy.



### Impact of Adalimumab (HUMIRA®) on Patient-Reported Outcomes among Patients with Fistulizing Crohn's Disease in the CHARM Trial

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**Purpose:** Fistulas occur in 17–43% of patients with Crohn's disease (CD), and fistulizing disease is associated with worsening quality of life. Complete and sustained fistula closure has been associated with adalimumab (ADA) therapy in the CHARM trial, a Phase III randomized, double-blinded, placebo-controlled assessment of ADA in maintaining clinical remission in patients with CD.[1]

**Methods:** We assessed the impact of ADA maintenance therapy on CD-specific health-related quality of life (HRQOL) among randomized patients with draining fistulas observed at screening visits and at baseline (BL) of the CHARM trial. Inflammatory Bowel Disease Questionnaire (IBDQ) evaluations were conducted at BL and at Weeks 4, 12, 26, and 56 of the CHARM trial. IBDQ scores over time between groups receiving ADA, 40 mg every other week (EOW) or 40 mg every week (EW), or placebo (PBO), were compared using analysis of covariance. The proportions of patients achieving  $\geq 16$ -point improvement in IBDQ from BL, the minimum clinically meaningful improvement, were compared using chi-square tests.

**Results:** The baseline CDAI and IBDQ were similar for fistulizing patients and non-fistulizing patients (mean CDAI: 314 vs. 311; IBDQ: 123 for both groups). Of 117 patients with fistulizing CD who entered the study, 75 had IBDQ measurements after Week 4 and were followed through Week 56. Statistically significant and clinically meaningful results observed with ADA maintenance were sustained through Week 56. Mean changes in IBDQ scores from BL and the percentage of patients achieving  $\geq 16$ -point improvement in IBDQ from BL at Week 56 are presented (table).

Change From Baseline IBDQ and % of Patients With  $\geq 16$ -Point Total IBDQ Gain at Week 56

Improvements from BL	PBO (N = 26)	40 mg ADA EOW (N = 21)	40 mg ADA EW (N = 28)
Total IBDQ (mean)	21.6	43.5*	46.8*
$\geq 16$ -point IBDQ (%)	46	76*	86**

\* $P < 0.05$ , \*\* $P < 0.01$ , both vs. PBO.

**Conclusion:** Adalimumab maintenance therapy is associated with sustained and clinically meaningful improvement of CD-specific quality of life among patients with fistulizing Crohn's disease as measured by the IBDQ. [1] Colombel JF, et al. *Gastroenterology*. 2007;132:52–65.

### Continuous vs. Induction Only/Reinitiated Adalimumab Maintenance Therapy Yields Optimal Results for Moderate to Severe Crohn's Disease: Subanalysis of CHARM

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**Purpose:** Fully human monoclonal antibody, adalimumab (ADA), with demonstrated efficacy and safety in CHARM, is approved for treating moderate to severe Crohn's disease (CD). In this subanalysis, we compared ADA efficacy of continuous maintenance therapy (CMT) vs. Induction Only/Reinitiation (IO/R) therapies.

**Methods:** In CHARM, 854 pts received ADA, 80 mg/40 mg at Weeks (Wks) 0/2. At Wk 4, 778 pts were randomized to receive ADA 40 mg every other week (EOW; N = 260) or weekly (EW; N = 257), or placebo (PBO; N = 261) through Wk 56. At/after Wk 12, pts could switch to open-label (OL) ADA 40 mg EOW and increase to EW for flare/non-response. Pts on OL EW could not de-escalate to EOW. ADA efficacy (remission [CDAI < 150], total IBDQ, fistula closure, flare occurrence, and hospitalization risk) was compared with CMT vs. IO/R—pts who received IO therapy followed by PBO, or pts randomized to PBO and later reinitiated on OL ADA. The CMT group included pts on randomized ADA who either remained on blinded therapy or subsequently went to OL. A Cox proportional hazard model, after stepwise confounder selection, estimated the effect of ADA on hospitalization risk, controlling for Wk-4 responder status, stenosis/stricture history, and age.

#### Results:

**Conclusion:** CMT ADA therapy resulted in significantly greater remission rates, quality of life improvements, fewer flares, and reduction in all-cause and CD-related hospitalizations vs. IO/R therapy. The preponderance and consistency of these analyses collectively suggest CMT with ADA yields superior results for pts with moderate to severe CD when compared with IO/R dosing.

### Feeding Decisions in Patients with Advanced Dementia – Formative Research

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**Purpose:** To understand feeding decisions in the elderly with late-stage dementia from perspectives of caregivers, primary-care physicians, gastroenterologists and nursing home staff, to guide strategies to improve care through informed, shared-decision making.

**Methods:** In-person interviews were held with caregivers, primary-care physicians, gastroenterologists and nursing home staff. A semi-structured interview was designed for each group. With caregivers, interviewers were particularly mindful of the need to not infer caregivers made “uninformed” decisions but focused on having them “tell their stories”. Notes were summarized by the two interviewers (DG and JZ).

CMT vs. IO/R at Wk 56

	IO/R	CMT-EW	CMT-EOW
Wk 56 CDAI (median)	183	154*	147*
Remission, n/N (%)	99/261 (38)	125/257 (49)*	132/260 (51)*
Total IBDQ, n (median)	261 (159)	257 (168)*	260 (168)*
Complete fistula closure, n/N (%)	13/33 (39)	20/31 (65)*	11/22 (50)
CD-related hospitalization***	Reference group	0.52 (0.32–0.83)**	0.63 (0.40–0.99)*
All-cause hospitalization***	Reference group	0.53 (0.36–0.78)**	0.55 (0.37–0.80)**
Flares (mean)	0.98	0.85*	0.80*

LOCF. \* $P < 0.05$  and \*\* $P < 0.01$  vs. IO/R. \*\*\*Hazards Ratio (95% CI).

**Results:** In discussions with caregivers, the theme of “starving to death” was clear and strong. Caregivers saw “no choice”, and a feeding tube is necessary “when it is time”. Hand-feeding was not discussed with caregivers as an option to tube-feeding. The primary-care physicians and geriatrician report few of their dementia patients have feeding tubes, indicating dissonance with general practice. All acknowledged poor efficacy of feeding tubes, “they may increase quantity, but not quality time.” “I often do not present the option of a feeding tube to patients.” A nursing home administrator felt it took less time to care for a patient with a feeding tube. He appeared uncomfortable when asked for the relative reimbursement rate for tube-feeding vs. hand-feeding. Interestingly, the nursing-home nurse stated that there is no time saved by tube-feeding when all skilled care is included. A gastroenterologist felt there was pressure from nursing homes to insert feeding tubes stating he acquiesced to a nursing-home previously on this issue. He noted that suggestion by a gastroenterologist toward not placing a feeding tube may be met with resistance by a family who has already made a decision for placement. He often feels “like a mechanic” and not an active participant in the decision-making process.

**Conclusion:** These pilot interviews reinforce issues of communication for individuals involved in feeding of elderly, late-stage dementia patients. Primary-care doctors have the challenge of communicating options in situations of emotion in the context of difficult decisions about prognosis. Gastroenterologists are often removed from the decision-making process, even though they have vast experience in feeding issues. A team-oriented approach, with more consideration of the primary-care challenge and gastroenterologist’s knowledge of nutrition and feeding, may help improve shared and informed decision-making.

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#### Characteristics and Outcomes of Gastroparesis-Related Hospitalizations in the United States, 2004

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**Purpose:** Gastroparesis is an increasingly recognized disorder in patients with nausea and vomiting. In a previous analysis, we found that gastroparesis-related hospitalizations increased 138 percent in the United States during 1995–2004 (DDW 2007; T1119). We aimed to examine the characteristics and outcomes of gastroparesis-related hospitalizations in 2004 and compare gastroparesis to common upper gastrointestinal (GI) conditions including gastroesophageal reflux disease, gastric ulcer, gastritis, and non-specific nausea/vomiting.

**Methods:** The publicly available Healthcare Cost and Utilization Project Nationwide Inpatient Sample 2004, a nationally representative sample of 8 million hospital stays, was used. Gastroparesis-related hospitalizations were defined as those with the primary diagnosis or a secondary diagnosis of gastroparesis (ICD-9-CM code 536.3). Multivariate regressions were used to control for age, sex, type of primary insurance, admittance through the emergency department, diabetic status, number of diagnoses, and/or number of procedures and compare differences in outcomes including length of stay, total charges, and in-hospital deaths.

**Results:** Of all gastroparesis-related hospitalizations (N = 29,083), 7 percent had gastroparesis as the primary diagnosis. Of hospitalizations with gastroparesis as a secondary diagnosis, the top 3 primary diagnoses were diabetes with neurological manifestations (24.0%), diabetes with ketoacidosis (5.9%), and congestive heart failure (2.8%). Compared to hospitalizations with a common upper GI condition as the primary diagnosis, hospitalizations with gastroparesis as the primary diagnosis were more likely to be diabetic (27% for gastroparesis vs. 14.2–21.0% for common upper GI conditions). The latter also had the longest length of stay (+15.4% to +66.2%, all  $P < 0.001$ ) and the highest or second highest total charges (-7.2% to +60.6%, all  $P < 0.01$ ) in multivariate regressions. In 2004, it was projected gastroparesis as the primary diagnosis led to 62,296 hospital days, \$208 million hospital charges, and 57 in-hospital deaths in the United States and that gastropare-

sis as a secondary diagnosis led to 849,667 hospital days, \$3,292 million hospital charges, and 1,709 in-hospital deaths.

**Conclusion:** Compared with common upper GI conditions, gastroparesis had the longest length of stay and the highest or second highest total charges. The economic impact of gastroparesis-related hospitalizations is significant in the United States.

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#### Administrative Data for Colonoscopy with Polypectomy Have a High Level of Accuracy

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**Purpose:** Guidelines from the ACG consider colonoscopy to be the procedure of choice for colorectal cancer screening. One method for monitoring the use of colonoscopy and associated polypectomy is through the use of administrative or billing data, which are typically recorded with Current Procedure Terminology 4th Edition (CPT-4) and International Classification of Diseases 9th Revision (ICD-9) codes. However, the accuracy of these codes for identifying polypectomy has not been validated in clinical practice. We hypothesized that colonoscopy with polypectomy billing codes as recorded by medical coders correlated well with the actual physician procedure report.

**Methods:** We used physician practice administrative data from 2002 and 2003 to select a random sample of 502 patients aged 65 and older with CPT-4 codes for colonoscopy with biopsy (N = 226), hot biopsy (N = 42) or polypectomy (N = 143). We included procedures performed at a freestanding ambulatory surgery center (ASC) as well as the endoscopy unit of a tertiary care hospital. The corresponding endoscopy reports were reviewed and considered to be the gold standard in the analysis. In addition, the pathology reports were reviewed and the predictive accuracy of various codes for identifying adenomatous polyps was determined. We measured the sensitivity (Sens) and positive predictive value (PPV) of the procedure codes.

**Results:** There was a high level of concordance between the physician billing codes and procedure notes for snare polypectomy (Sens 99%, PPV 100%), biopsy (Sens 98%, PPV 95%) and hot biopsy (Sens 82%, PPV 93%). To identify adenomas 5 mm or greater, codes for snare had the highest accuracy (Sens 75.5%, PPV 82.6%), followed by hot bx (Sens 16%, PPV 80.9%) and cold bx with polyp diagnosis (Sens 6.9%, PPV 13.4%). To identify adenomas of size 10 mm or greater, snare polypectomy codes had a Sens and PPV of 98.3% and 88%, respectively, with the sample size too small for cold and hot bx. No differences in accuracy were noted between the two practice sites.

**Conclusion:** In this two facility study, billing codes have high level of accuracy for identification of colonoscopy with biopsy, hot biopsy and snare polypectomy. In addition, codes for snare polypectomy have the highest accuracy for identification of large adenomas. These data support the use of administrative data for studies of the use of colonoscopy and its applications.

## INFLAMMATORY BOWEL DISEASE

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#### Beclomethasone Dipropionate + Mesalamine Enemas for Refractory Ulcerative Proctitis. A Retrospective Analysis

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**Purpose:** Active ulcerative proctitis is usually treated with local administration of either mesalamine or corticosteroids. Cessation of rectal bleeding can be already observed within a couple of weeks, but occasionally patients do not respond to standard local therapy.

Purpose of our analysis was to establish the therapeutic role of enemas combining mesalamine and beclomethasone dipropionate in patients resistant to rectal administration of beclomethasone dipropionate alone

**Methods:** We re-examined retrospectively 34 outpatients with rectal localization of ulcerative colitis treated in our Unit during the last four years. The subjects, aged 29–47 years, had experienced a clinical flare-up of the disease during oral maintenance with mesalamine 1600 mg daily and had been treated with rectal beclomethasone dipropionate 3 g/100 ml at bedtime for up to 15 days with persistence of rectal bleeding.

Sixteen patients continued the ongoing local treatment with beclomethasone enemas for further two weeks and increased the oral dose of mesalamine to 3.200 mg daily (group A). The remaining eighteen subjects maintained oral mesalamine 1.600 mg daily and were treated for two weeks at bedtime with a rectal enema where beclomethasone 3 g/100 was mixed with a powder containing 1.5 g of mesalamine (group B).

**Results:** In group A, five patients reported no more bleeding at the end of the treatment period, whereas eleven patients with persistent bleeding at two weeks were switched to oral corticosteroids.

In group B sixteen of the eighteen subjects experienced disappearance of rectal bleeding.

The difference between the two treatment groups is statistically significant:  $P = 0.002$  by chi-square test

**Conclusion:** Our preliminary, retrospective analysis suggests that: 1) rectal administration of a mixture of beclomethasone and mesalamine is effective in patients refractory to rectal beclomethasone alone; 2) adding rectal mesalamine to the beclomethasone enema is more effective than increasing the dose of oral mesalamine.

## 927

### Rifaximin Improves Symptoms in Patients with Crohn's Disease or Ulcerative Colitis

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**Purpose:** Inflammatory bowel disease (IBD) is a chronic intestinal disorder with multiple etiologies. In IBD, including disease refractory to standard first-line therapies, inflammation is likely caused by an exaggerated immune response to commensal enteric bacteria in genetically predisposed individuals, suggesting that antibiotic therapy may be beneficial. Systemic antibiotics and immunomodulators are frequently administered to treat IBD. However, systemic antibiotics may not adequately target the intestinal lumen, and immunomodulators do not affect the underlying pathogenic cause of the disease. Rifaximin is a nonsystemic, gastrointestinal-specific antibiotic that provides targeted treatment to resolve bacterial insult and improve IBD symptoms.

**Methods:** This retrospective chart review evaluated outcomes in patients with mild-to-moderate refractory Crohn's disease (CD) or ulcerative colitis (UC) who received adjunctive therapy with rifaximin 400 mg 3 times daily for 2 to 4 weeks during the period from the end of 2004 through 2005. Chart reviews assessed disease location, previous antibiotic therapy, concomitant medications, clinical response (>50% symptom improvement) or clinical remission (100% symptom resolution) after initiation of rifaximin treatment, and incidence of adverse effects.

**Results:** Fourteen adult patients were identified (mean age, 43 y); 3 patients had UC and 11 patients had CD. Eleven patients (79%) had received treatment with systemic antibiotics in the previous 2 weeks. Prior to rifaximin treatment, 10 patients had been taking immunomodulators, 13 had been taking oral mesalamine, and 5 had been taking oral steroids, all with suboptimal results. Thirteen patients (93%) had a clinical response with rifaximin, and 9 of these 13 responders (69%) experienced complete remission of IBD symptoms. Median time to complete remission after initiation of rifaximin treatment was 10 days. A higher rate of clinical remission was observed in patients with IBD localized to the colon (6 of 7 patients) or ileocolon (3 of 4 patients) versus the ileum (0 of 3 patients). Concomitant treatments were well tolerated, with only 2 reports of nausea and 1 report each of flatulence, dyspepsia, and headache, none of which resulted in treatment discontinuation.

**Conclusion:** These findings suggest that rifaximin 1200 mg/d for up to 4 weeks is a potentially beneficial therapy for patients with IBD. Large, well-designed, controlled trials are warranted to confirm these promising preliminary clinical findings.

## 928

### Gender Influences Time to Diagnosis for Patients with Crohn's Disease Confined to the Ileum

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**Purpose:** Crohn's Disease (CD) is an idiopathic inflammatory disease that can occur anywhere along the digestive tract, with one-third of cases limited to the distal ileum. CD of the terminal ileum causes non-specific symptoms that can easily be mistaken for other conditions, including Irritable Bowel Syndrome (IBS). Our aims were to assess for differences in time to diagnosis between women and men with CD limited to the terminal ileum as well as quantify the number of diagnostic tests until correct diagnosis for both sexes.

**Methods:** This was a single-center, retrospective study. Thirty-five women with Crohn's disease limited to the terminal ileum were matched by age of diagnosis with 40 men also with disease limited to the terminal ileum. Patients with any colonic or perianal disease, or who presented with acute perforation or obstruction were excluded. Symptoms, time to diagnosis from symptom onset, number of physician visits and number of diagnostic tests performed were recorded.

**Results:** There was no difference between men and women for the age at onset of symptoms. There was a significant difference for the length of time of undiagnosed symptoms for women compared to men (76.7 months vs. 35.5 months,  $P = 0.007$ ). Women were also more likely to have undiagnosed symptoms for more than 36 months prior to diagnosis (OR = 3.9, 95% CI = 1.23–12.4). Women were found to be at greater risk of undergoing more than 3 diagnostic tests prior to diagnosis (OR = 4.2, 95% CI = 1.25–14.1), and for undergoing more diagnostic tests than men (3.85 vs. 2.55 tests,  $P = 0.01$ ).

**Conclusion:** Women are diagnosed significantly later after symptom onset than men and undergo more diagnostic tests before CD is diagnosed. Work up for gastrointestinal complaints should include full assessment of the small intestine before a diagnosis of IBS is made.

	Women (N = 35)	Men (N = 40)	P-value
Mean age at sx onset yrs (SD)	22.5 (4.2)	23.6 (5)	NS
Mean time from symptom onset to diagnosis (months)	76.7	35.5	0.007
Time of undiagnosed symptoms > 36 mo	46.4%	18.2%	0.026
Mean # diagnostic tests done pre-diagnosis	3.86	2.55	0.01

## 929

### The Different Expression of Pro-Inflammatory Cytokines and a Pro-Apoptotic Protein, in Pelvic Ileal Pouches for Ulcerative Colitis and Familial Adenomatous Polyposis

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**Purpose:** Pouchitis after total colectomy is the commonest complication in ulcerative colitis (UC), while is quite rare in familial adenomatous polyposis (FAP).

**Objective:** To evaluate the inflammatory activity in endoscopically normal ileal pouch mucosa, by determining the expressions of IL-1 $\beta$ , IL-6, IL-8, TNF- $\alpha$ , a pro-apoptotic protein p-Bad, and the activation of NF-KB in patients with UC and FAP.

**Methods:** Twenty patients submitted to total colectomy and J pouch, asymptomatic, were evaluated, 10 patients with UC and 10 with FAP. The control group consisted of ten individuals with normal ileo-colonoscopy examinations. The specimens were snap-frozen in liquid nitrogen and the expressions of TNF- $\alpha$ , IL-1 $\beta$ , IL-6, IL-8 and p-Bad were determined by immunoblot of total protein extracts. NF-KB was evaluated by immunoprecipitation and immunoblot. The absence of pouchitis was assessed clinically, histology and endoscopically, according to the Pouchitis disease activity Index. All biopsies were taken after the approval by regional ethic commit, and informed consent from the patients.

**Results:** TNF- $\alpha$ , IL-1 $\beta$ , IL-6, IL-8 and p-Bad expression was increased in patients with UC, when it was compared with FAP ( $P < 0.05$ ). Otherwise, NF-KB activation was similar in both groups. The control group had little TNF- $\alpha$  expression ( $P < 0.01$ ) when compared with UC and FAP. There were no statistical difference in NF-KB activation ( $P > 0.1$ ) and IL-1 $\beta$ , IL-6, IL-8 and p-Bad expressions ( $P > 0.05$ ) when compared control group with UC and FAP.

**Conclusion:** This study is important because there are, to our knowledge, few studies that evaluated inflammatory activity in asymptomatic ileal pouches, and whether there is any relationship with pro-apoptotic proteins. The patients with UC had increased levels of the studied cytokines, even without clinic and endoscopic evidence of pouchitis. Moreover, there was increased p-Bad expression. These findings may suggest a higher susceptibility to this inflammatory complication in patients with UC, and could explain the increased epithelial cell apoptosis, that could correlates with the mucosa atrophy in patients with pouchitis.

## 930

**Biological Therapy with Infliximab in Ulcerative Colitis:****Personal Experience**

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**Purpose:** Clinical experience of therapy with Infliximab in patients with Ulcerative Colitis (UC) is still not well known. We report our personal experience with Infliximab in 3 patients with UC not responder or dependent to high dosage of steroid therapy.

**Methods:** 3 male patients with UC were enrolled. G.E., 7 years, presented iperacute UC (pre-mega toxic colon stage) not responder to steroid treatment. C.D., 9 years, dependent to high dosage of steroid and with arthralgic symptoms and functional limitations not improved by metothrexate. I.V., 16 years, dependent to high dosage of steroid and not improved by azathioprine started 6 months before. The classic therapeutic scheme with induction remission therapy followed by maintenance therapy at 5 mg/kg/dose was administrated intravenously. All patients took steroids and antihistamine therapy 3 days before the infusion and steroid was administrated intravenously just before the infusion of Infliximab.

**Results:** In the first patient a progressive improvement of pre-mega toxic colon permitted to avoid an urgent surgery. After 3 Infliximab infusions a viral infection worsened general conditions and abdominal symptoms, determining the necessity of surgery in election with colectomy by Soave with ileo-ano anastomosis and ileostomy, after 15 days from the last infusion. Now the patient, after reconstitution of intestinal continuity, is in good general condition and asymptomatic. In the second patient therapy with Infliximab determined a complete clinical endoscopic/histological remission of

UC and a complete remission of arthralgias after 3 infusions. This patient is still receiving biological therapy. In the third patient after 3 months from last Infliximab infusion a rectal-sigmoidal relapse of UC was observed although he is still in therapy with azathioprine.

**Conclusion:** Infliximab therapy in patients with UC is effective, but we don't know if and how it can condition the future natural course of the disease. In one patient, Infliximab therapy was effective as a "bridge drug" to avoid urgent surgery but it was not able to avoid surgery in election. In the second patient it was useful to control the intestinal and arthralgic symptoms but the evolution after the suspension of the therapy is not foreseeable. In the last patient Infliximab well controlled the iperacute disease but after 3 months from the last infusion a mild relapse occurred.

## 931

**Exposing the Weaknesses: A Systematic Review of Azathioprine Efficacy in Ulcerative Colitis**

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**Purpose:** We performed a systematic review and meta-analysis to evaluate the clinical efficacy of azathioprine or 6-mercaptopurine after standard induction with corticosteroids. We also sought to explore potential sources of clinical trial heterogeneity that may have influenced the results of previous trials.

**Methods:** A comprehensive search of online databases was conducted. Only randomized controlled trials with azathioprine or 6-mercaptopurine within a minimum duration of follow-up of 6 months were selected. Pooled relative risk estimates were calculated for the primary outcome "success of treatment", defined as clinical remission or significant clinical response or failure to relapse.

**Results:** In total, 6 trials were included in the systematic review and 5 in the meta-analysis. The pooled relative risk estimate, using a random effects model, for "success of treatment" with AZA compared to 5-ASA and/or placebo was 1.42 (95% CI 0.93–2.17,  $P = 0.109$ ). Using only trials of higher methodology quality (Jadad score  $> 2$ ), the pooled relative risk estimate was 2.05 (95% CI 1.30–3.23,  $P = 0.002$ ).

**Conclusion:** In summary pooling the results of the two trials of highest methodologic quality demonstrated a modest efficacy of azathioprine compared to 5-ASA and/or placebo for the successful treatment of ulcerative colitis. These results must be interpreted with caution as they are based on two relatively small trials. Therefore, although the use of azathioprine is common in the management of UC this practice is not based on high quality evidence.

## 932

**Mycobacterium Paratuberculosis in Crohn's Disease Granulomas**

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**Purpose:** Crohn's disease is a chronic inflammatory bowel disease of as yet unknown and possibly heterogeneous aetiology. A possible infectious aetiology has also been repeatedly discussed. One of the most plausible candidates is *Mycobacterium avium* subspecies paratuberculosis (MAP). Numerous authors have explored the link between MAP and Crohn's disease using various methods on biopsies, resections, fresh, frozen, and paraffin-embedded tissue, with variable results.

**Aim:** To examine the detection rate of MAP in patients with Crohn's disease using paraffin-embedded tissues and a semi-nested IS900 specific PCR.

**Methods:** Paraffin-embedded tissues of patients with Crohn's disease were analyzed. Microdissection of granulomas and peri-granulomas (normal) was performed. On the basis of sequence reported in GenBank alignments, we

designed primer sets specific for *M. avium* subsp. *paratuberculosis*. The presence of the MAP was examined by semi-nested IS900 specific PCR.

**Results:** Human beta-actin gene was amplified in all cases, indicating successful DNA quality. Detection rate of MAP specific IS900 DNA by PCR was appropriately identified from two controls (paraffin-embedded tissue and bacteria culture) confirming the specificity and sensitivity of designed primers. The presence of MAP was found in 1/20 (5%) patients with Crohn's disease; in this case the semi-nested PCR targeting IS900 was positive in microdissected granuloma.

**Conclusion:** We designed a PCR assay that permits the detection of short DNA fragments of the MAP specific IS900 gene in paraffin-embedded samples. Furthermore, the use of microdissection permitted to detect MAP DNA in granulomas in one patient with Crohn's disease. Detection of MAP DNA within granuloma might suggest an infectious etiology in a small subset of patients with Crohn's disease.

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933

#### Surveillance Pouch Endoscopy for the Detection of Dysplasia in Ulcerative Colitis Patients with Ileal-Pouch Anal Anastomoses Is Cost-Effective (IPAA)

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**Purpose:** Dysplasia or cancer can still occur in the anal transitional zone (ATZ) or ileal pouch mucosa after IPAA for ulcerative colitis (UC). Whether surveillance pouch endoscopy is needed is controversial. The aim of the study is to evaluate the cost-effectiveness of pouch endoscopy with different surveillance strategies using Markov decision-tree models.

**Methods:** The target population was adult IPAA patients with underlying UC. One year was used as the transitional cycle in the model. The yearly transitional probabilities, i.e., the annual incidences, were derived from a literature review. A hypothetical population size of 1000 with an average starting age of 40 was followed for 30 years. Only costs associated with surveillance (from payers' perspective) were considered. The effectiveness outcome in the analysis is measured in person-year that surveillance would advance the diagnosis of dysplasia. High-risk patients were defined as those with chronic pouchitis; severe villous atrophy of pouch mucosa; cuffitis; primary sclerosing cholangitis; pre-operative diagnosis of backwash ileitis, dysplasia or cancer; and family history of colon cancer. The cost-effectiveness threshold of \$50,000 per life-year was applied for the decision analysis.

**Results:** The estimated incidence rates for dysplasia of any grade in the ATZ or pouch mucosa were 0.34% and 1.93% for average-risk and high-risk patients, respectively. Sensitivity analysis was conducted within the ranges specified for costs and annual incidences. The surveillance strategy is very sensitive to the estimated annual incidence.

**Conclusion:** Surveillance pouch endoscopy is cost-effective for average-risk patients (Q 3 yrs) and for high-risk patients (Q 1 yr), which was sensitive to change in incidence rates.

934

#### The Influence of Immune Modifier Therapy on the Development of Non-Melanoma Skin Cancer in Patients with Crohn's Disease under Age Fifty

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**Purpose:** A few case reports have identified the use of immune suppressive drugs for treatment of inflammatory bowel disease as a risk for the development of skin cancer. Non-melanoma skin cancer (NMSC) is more common in men and usually occurs in those older than age 50. The aim of this study was to investigate the relationship of NMSC to immune suppression therapy among patients with Crohn's disease less than age 50.

**Methods:** With IRB approval, a retrospective chart review of patients at Mayo Clinic, Rochester, MN, who had documented CD diagnosed between 1975 and 2004 and who were subsequently diagnosed with NMSC. Inclusion criteria were: age less than 50 at the time of skin cancer diagnosis; diagnosis of skin cancer at least 2 years after CD diagnosis; no prior history of skin cancer or pre-malignant skin disease; and residence in Minnesota, Iowa, Illinois, Wisconsin, N. Dakota, or South Dakota.

**Results:** 15 patients (7 Caucasian males, 8 Caucasian females), who met the inclusion criteria were identified: 7 received either no medical therapy or only mesalamine for CD prior to developing NMSC while 8 received immune suppressive drugs (steroids only = 2, Azathioprine/6-MP = 6). None of the patients had received infliximab or other biologic therapies. The median ages for those who did not and those who did receive immune suppression were 43 years and 46 years, respectively,  $P = 0.327$ . The median time from diagnosis of CD to diagnosis of NMSC was 14.1 years in the group receiving no immune suppressives and 15.5 years in the immune suppressive group,  $P = 0.921$ . All 7 patients (4 males, 3 females) who did not take immune suppressives developed basal cell carcinomas (BCCs), and 2 also developed squamous cell cancers (SCC). Among the 8 patients (3 males, 5 females) who took immune suppressives, 6 developed SCCs (2 also had BCCs), and 2 other patients had BCCs only. No patient developed more than 2 NMSCs over the study period.

**Conclusion:** Among patients with Crohn's disease who developed non-melanoma skin cancer before age 50, there was no gender predominance, and treatment with immune suppression was not associated with an increased risk of skin cancer.

935

#### MMX<sup>TM</sup> Mesalamine Is Effective for the Maintenance of Remission of Mild-to-Moderate Ulcerative Colitis Irrespective of Patients' Previous Relapse History

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Cost-effectiveness Analysis of Surveillance for dysplasia (N = 1000, T = 30 years):

	Total Cost (C, million\$)	Person-year Advanced Dx of Dysplasia (E)	Incremental Cost-Effectiveness ratio, \$ per person-year
No surveillance, average/high risk	0/0	0/0	NA
Q 10 yr surveillance, average/ high	1.6/1.6	1006/4994	1,596/322
Q 5 yr surveillance, average/high risk	3.2/3.2	1254/6153	6,475/1,385
Q 3 yr surveillance, average/high risk	5.4/5.4	1353/6607	21,668/4,717
Q 2 yr surveillance, average/high risk	8.0/8.0	1402/6832	54,264/11,906
Q 1 yr surveillance, average/high risk	16.1/16.1	1451/7055	162,978/35,974

**Purpose:** To investigate the effect of relapse history in patients with mild-to-moderate ulcerative colitis (UC) on the efficacy of maintenance therapy with MMX Multi Matrix System® (MMX) mesalamine (LIALDA™ [MEZAVANT™ XL in the UK and Ireland, MEZAVANT™ elsewhere]).

**Methods:** Patients with active, mild-to-moderate ulcerative colitis (UC) in two phase III, randomized, placebo-controlled studies (SPD476–301 and -302), received MMX mesalamine 2.4 or 4.8 g/day, or placebo, for 8 weeks. An ASACOL® (mesalamine) delayed-release tablet (Procter & Gamble Pharmaceuticals, Cincinnati, OH, USA) 2.4 g/day internal reference arm was also included in study 302. Patients not in remission after study 301 or 302 could receive an additional 8 weeks' high-dose (4.8 g/day) MMX mesalamine therapy as part of a long-term, open-label study (SPD476–303). Patients in remission at the end of study 301, 302 or the 8-week extension phase of 303 could enter the 303 maintenance phase and receive MMX mesalamine 2.4 g/day for 12 months. Remission was defined as a modified UC Disease Activity Index score of  $\leq 1$ , calculated as: rectal bleeding and stool frequency scores of 0, a combined Physician's Global Assessment score and sigmoidoscopy score of  $\leq 1$ , no mucosal friability; and  $\geq 1$ -point reduction in sigmoidoscopy score from baseline.

**Results:** 438 evaluable patients with complete relapse records prior to the parent studies' baseline entered the 12-month maintenance phase. Overall, 290 patients (66%) achieved remission at 12 months. Of patients who previously experienced  $<3$  relapses in the two years prior to parent study baseline, 70.1% (192/274) achieved remission at 12 months. In comparison, 59.8% (98/164) of patients who previously experienced  $\geq 3$  relapses in the two years prior to parent study baseline achieved remission at 12 months.

**Conclusion:** Relapse history may identify patients with difficult-to-control UC in whom long-term remission rates may be reduced. Nevertheless, about 60% of patients who experience  $\geq 3$  relapses in the two years prior to receiving treatment with MMX mesalamine are likely to be in remission up to one year later when receiving MMX mesalamine 2.4 g/day maintenance therapy. Further studies are needed to determine if a higher maintenance dose of MMX mesalamine is warranted in patients who are prone to relapse.

## 936

#### MMX™ Mesalamine Is Effective for the Maintenance of Ulcerative Colitis Remission in Both Left-Sided and Extensive Disease

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**Purpose:** A combined analysis of two phase III, placebo-controlled studies (SPD476–301 and -302) has demonstrated mesalamine with MMX Multi Matrix System® (MMX) technology (LIALDA™, also known as MEZAVANT™ XL in the UK and Ireland, and as MEZAVANT™ elsewhere; hereafter referred to as MMX mesalamine) to be efficacious for the induction of remission of active, mild-to-moderate ulcerative colitis (UC), in patients with left-sided (distal to the splenic flexure) or extensive (involving the transverse colon) disease. In a subsequent 12-month extension study (SPD476–303), MMX mesalamine 2.4 g/day has demonstrated efficacy for maintenance of UC remission. Here we present a post-hoc analysis of 12-month remission rates with MMX mesalamine therapy in patients with a medical history of either left-sided or extensive UC.

**Methods:** Patients were randomized to MMX mesalamine 2.4 g/day given once daily (QD) or 1.2 g given twice daily (BID) for 12 months. Remission was defined as a modified Ulcerative Colitis Disease Activity Index score  $\leq 1$ , calculated as: scores of 0 for rectal bleeding and stool frequency, a combined Physician's Global Assessment and sigmoidoscopy score of  $\leq 1$ , no mucosal friability, and a sigmoidoscopy score reduction of  $\geq 1$  from baseline.

**Results:** In total, 451 patients were included in the efficacy population. Of the 450 with known extent of disease, 67.0% (233/348) and 64.7% (66/102) of

patients with left-sided or extensive disease, respectively, were in remission at month 12. The results were similar with once- or twice-daily treatment in patients with left-sided (QD = 65.5%, BID = 68.4%,  $P = 0.570$ ) or extensive disease (QD = 60.4%, BID = 68.5%,  $P = 0.393$ ).

**Conclusion:** MMX mesalamine 2.4 g/day is effective for the maintenance of remission of mild-to-moderate UC in both left-sided and extensive disease.

## 937

#### Long-Term Remission Rates in Patients with Mild-to-Moderate Ulcerative Colitis Who Require an MMX™ Mesalamine Dose Increase To Induce Initial Remission

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**Purpose:** MMX Multi Matrix System® (MMX) mesalamine (LIALDA™ [US] MEZAVANT™ XL [UK and Ireland] and MEZAVANT™ [elsewhere]), is a novel high-strength, once-daily 5-aminosalicylic acid therapy that has been shown to be efficacious for the induction and maintenance of remission of mild-to-moderate ulcerative colitis (UC) in a phase III clinical trial program. Here we examine long-term remission rates in patients who required a MMX mesalamine dose escalation to induce remission.

**Methods:** In two placebo-controlled, phase III clinical trials (SPD476–301 and -302), patients with active, mild-to-moderate UC received MMX mesalamine 2.4 or 4.8 g/day for up to 8 weeks to induce remission. Those patients not in remission at the end of these trials could opt to receive a further 8 weeks' treatment with MMX mesalamine 4.8 g/day (as part of a two-phase, open-label trial [SPD476–303]). Patients who achieved remission in these studies could choose to receive MMX mesalamine 2.4 g/day maintenance therapy for 12 months (second phase of study 303). In this retrospective analysis, we determined 12-month remission rates for (a) patients who received MMX mesalamine 2.4 g/day as induction therapy and then entered the maintenance study directly; and (b) patients who received 2.4 g/day plus a further 8 weeks of high-dose MMX mesalamine therapy before entering the maintenance phase (2.4 g/day).

**Results:** Seventy-nine patients received MMX mesalamine 2.4 g/day in studies 301 and 302 and entered the maintenance phase directly. A total of 53 patients received MMX mesalamine 2.4 g/day for 8 weeks, plus a further 8 weeks' MMX mesalamine 4.8 g/day and then entered the 12-month maintenance phase of study 303. Twelve-month remission rates were 73.4% for patients who directly entered the maintenance phase, and 50.9% for those who entered via the 8-week extension phase.

**Conclusion:** In this analysis, in patients initially treated with MMX mesalamine 2.4 g/day, the requirement for further treatment at a higher dose to achieve remission was associated with reduced long-term remission rates. These patients may represent a difficult-to-treat subgroup who may require a higher maintenance dose of MMX mesalamine. Further studies are needed to test this hypothesis.

## 938

#### Time to Initial Symptom Resolution with MMX™ Mesalamine Therapy for Active, Mild-to-Moderate Ulcerative Colitis

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**Purpose:** An important endpoint for both patients and physicians when treating active, mild-to-moderate ulcerative colitis (UC) is the time between

initiation of therapy and initial symptom resolution. Here we present the median time to initial resolution of rectal bleeding and normalization of stool frequency from a post-hoc analysis of pooled data from two phase III, placebo-controlled, double-blind, double-dummy studies (SPD476–301 and -302) of MMX Multi Matrix System<sup>®</sup> (MMX) mesalamine (LIALDA<sup>™</sup> [MEZAVANT<sup>™</sup> XL in the UK and Ireland, MEZAVANT<sup>™</sup> elsewhere]).

**Methods:** Patients with active, mild-to-moderate UC were randomized to MMX mesalamine 2.4 g/day (given once or twice daily) or 4.8 g/day (given once daily) or placebo, for 8 weeks. Time to initial resolution of symptoms (i.e. resolution of rectal bleeding, normalization of stool frequency, or both combined) was defined as the time between first dose of study medication and the first day of symptom resolution (defined for rectal bleeding and stool frequency as a score of 0).

**Results:** A total of 517 patients were included in the intent-to-treat population. Median time to resolution of symptoms (stool frequency and rectal bleeding) was 25, 26 and 44 days, in the MMX mesalamine 2.4 g/day, 4.8 g/day and placebo groups, respectively (Kaplan-Meier log-rank test:  $P = 0.0001$ ). For the resolution of rectal bleeding median times were 7, 8, and 16 days, respectively (Kaplan-Meier log-rank test:  $P < 0.0001$ ). For the normalization of stool frequency median times were 19, 20, and 34 days, respectively (Kaplan-Meier log-rank test:  $P = 0.0001$ ).

**Conclusion:** Once- or twice-daily MMX mesalamine offers initial resolution of UC symptoms within weeks of starting the medication.

## 939

### Once- or Twice-Daily MMX<sup>™</sup> Mesalamine for the Maintenance of Remission of Mild or Moderate Ulcerative Colitis

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**Purpose:** Mesalamine with MMX Multi Matrix System<sup>®</sup> (MMX) technology (LIALDA<sup>™</sup>, also known as MEZAVANT<sup>™</sup> XL in the UK and Ireland, and as MEZAVANT<sup>™</sup> elsewhere) is a novel, high-strength formulation of 5-aminosalicylate (5-ASA; 1.2 g per tablet), designed to release 5-ASA throughout the colon. An analysis of combined data from two randomized, phase III trials (SPD476–301 and -302) demonstrated the efficacy of MMX mesalamine for improving remission rates in patients with active, mild (Ulcerative Colitis Disease Activity Index [UC-DAI] score 4–<6) or moderate ulcerative colitis (UC-DAI score 6–10). In a subsequent 12-month extension study (SPD476–303), in patients achieving remission, MMX mesalamine 2.4 g/day was shown to be efficacious for maintenance of remission. Here, data from study 303 were analyzed to assess the efficacy of MMX mesalamine for the maintenance of remission in patients with either mild or moderate ulcerative colitis.

**Methods:** Patients were randomized to receive MMX mesalamine 2.4 g/day (given once daily [QD]) or 2.4 g/day (1.2 g given twice daily [BID]). Data were analyzed to assess remission rates by baseline disease severity. Remission at 12 months was defined as a modified UC-DAI score of  $\leq 1$  calculated as: rectal bleeding and stool frequency scores of 0, a combined Physician's Global Assessment and sigmoidoscopy score of  $\leq 1$ , no mucosal friability, and  $\geq 1$ -point reduction in sigmoidoscopy score from baseline.

**Results:** In the efficacy population ( $N = 451$ ), 12-month remission rates were 70.5% (117/166) for patients with mild disease at baseline, and 64.2% (183/285) for patients with moderate disease at baseline. Remission rates were not significantly different in patients receiving MMX mesalamine 2.4 g/day QD or BID for mild disease (69.0 vs 72.2%,  $P = 0.653$ ) or moderate disease (61.4 vs 66.7%,  $P = 0.352$ ).

**Conclusion:** MMX mesalamine 2.4 g/day, given QD or BID, is efficacious for the maintenance of remission of both mild and moderate ulcerative colitis.

## 940

### The Effect of Prolonged Therapy with MMX<sup>™</sup> Mesalamine in Patients with Acute, Mild-to-Moderate Ulcerative Colitis

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**Purpose:** MMX mesalamine (LIALDA<sup>™</sup> [US] MEZAVANT<sup>™</sup> XL [UK & Ireland] MEZAVANT<sup>™</sup> [elsewhere]), a novel, high-strength formulation of 5-aminosalicylic acid (5-ASA), has demonstrated induction of remission of mild-to-moderate ulcerative colitis (UC) in two phase III, placebo (pb)-controlled studies (SPD476–301 and -302 [parent studies]). The purpose of this analysis was to determine the proportion of patients (pts) not responding to acute treatment in these parent studies who could achieve remission in an 8-week extension study.

**Methods:** Pts in the parent studies received MMX mesalamine 2.4 g/d (once daily [QD; 302] or 1.2 g twice daily [BID; 301]), 4.8 g/d (QD [301 and 302]), ASACOL<sup>®</sup> (mesalamine) delayed-release tablets (Procter & Gamble Pharmaceuticals, Cincinnati, OH, USA) 2.4 g/d (0.8 g three times daily [TID; 302]) or pb [301 and 302] for 8 weeks. Pts not in remission after the parent studies could receive an additional 8 weeks' high-dose (4.8 g/d [2.4 g BID]) MMX mesalamine therapy in the extension phase of this open-label trial (SPD476–303). Remission rates (modified UC Disease Activity Index score of  $\leq 1$ , calculated as: rectal bleeding and stool frequency scores of 0; a combined Physician's Global Assessment and sigmoidoscopy score of  $\leq 1$ ; no mucosal friability; and  $\geq 1$ -point reduction in sigmoidoscopy score from baseline) were calculated at week 8 of the extension study.

**Results:** A total of 304 pts entered the 8-week extension phase and were included in the efficacy population. Overall, 59.5% of pts achieved stringently defined remission. Remission rates were similar regardless of previous treatment in the parent studies: pb = 57.0%; MMX mesalamine 2.4 g/d (QD or BID) = 61.5%; MMX mesalamine 4.8 g/d (QD) = 60.3%; ASACOL 2.4 g/d (0.8 g TID) = 61.0%.

**Conclusion:** An additional 8 weeks' MMX mesalamine therapy was able to induce stringently defined remission in a large proportion of pts failing an initial 8 weeks of 5-ASA therapy. Some pts may therefore avoid therapeutic escalation by continuing 5-ASA treatment beyond 8 weeks; although further studies are required to confirm this.

## 941

### Predictors of 5-ASA Prescription Persistence during the Chronic Phase in Patients with Ulcerative Colitis (UC)

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**Purpose:** To identify predictive factors for 5-ASA non-persistence in patients with UC (defined as no 5-ASA refill at 12 mos).

**Methods:** This retrospective cohort study used records of health service utilization from the Thomson Medstat MarketScan<sup>®</sup> research database. Treatment initiation (index date) was defined as 5-ASA use between Oct 2002–Sept 2004 with no 5-ASA use in the prior 6 mos. Study subjects were patients  $\geq 18$  years of age with a diagnosis of UC (ICD-9:556) in the period of interest and had refilled their prescription at 3 mos post index date. Subsequent 5-ASA prescription refill activity was captured at 12 mos; chronic keepers were defined as individuals who refilled their 5-ASA prescription at 12 mos ( $\pm 30$  days) whereas quitters did not refill at 12 mos ( $\pm 30$  days). Parameters of interest were captured from the 3 mo time point until the 12 mo time point and compared between keepers and quitters. Logistic regression modeling was used to identify independent predictors of non-refill persistence.

**Results:** 2,044 UC patients with 5-ASA prescriptions were identified; 920 patients (45%) did not refill their 5-ASA at 12 mos. GI hospitalization, co-morbid illness, mail order, and younger age were among the parameters significantly associated with non-persistence. Factors not found to be significantly associated with persistence were gender, endoscopy, psychiatric history, steroid or immuno-modulator use, number of GI office visits, and non-UC concomitant medications.

Significant Factors Associated with Risk of Not Refilling 5-ASA at 12 Months

	Parameters	Odds Ratio	P-value
Higher risk of not refilling	GI hospitalization (6.3%)	1.59	0.02
	Mail order of 3-month script (16.5%)	1.50	0.001
	Co-morbid conditions	1.04	<0.0001
Lower risk of not refilling	Age (per 1 year increase)	0.99	0.02
	Use of rectal 5-ASA (16.7%)	0.63	0.0004
	Switched to a different 5-ASA (7.7%)	0.53	0.0008

<sup>a</sup>Parentheses denote the percentage of total study population with specific characteristic

**Conclusion:** Persistence of maintenance therapy among UC patients taking 5-ASAs is multifactorial, though the factors related to persistence during the chronic disease phase differ somewhat from those of the acute phase, particularly sex and psychiatric history. Clinical knowledge of these factors can help with patient management.

942

#### Rapid Clinical Remission Is Significant for the Well-Being of Ulcerative Colitis Patients Treated with Delayed-Release Mesalamine

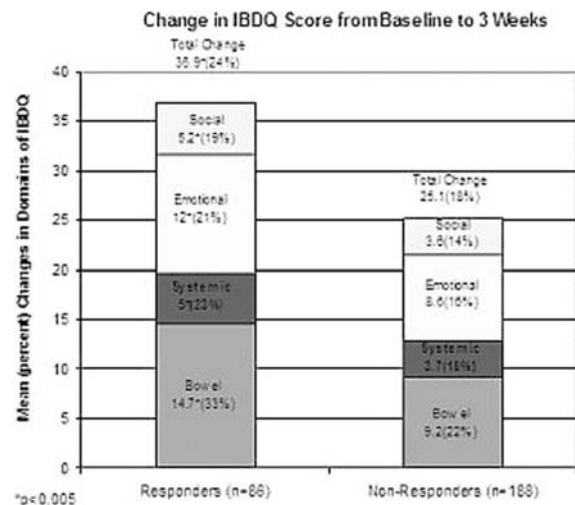
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**Purpose:** Rapid improvement in bowel symptoms is a key treatment goal for ulcerative colitis patients experiencing a flare, and has important implications for overall patient satisfaction with treatment. However, there is a paucity of data reporting quality of life benefits for the patient achieving rapid clinical remission.

The purpose of this analysis is to quantify the improvement in social, emotional, systemic, and bowel domains associated with clinical remission at 3 weeks using the Inflammatory Bowel Disease Questionnaire (IBDQ).

**Methods:** Combined data from two large multi-center, randomized, double-blind, active-controlled trials of similar design (ASCEND I & II) were analyzed for mildly and moderately active UC patients treated with Asacol (mesalamine) delayed-release tablets 2.4 g daily and who completed the IBDQ at 3 weeks after initiation of therapy (N = 274). Clinical remission was defined as patients achieving both a rectal bleeding score = 0 and a stool frequency score = 0 at 3 weeks. The change in IBDQ scores from baseline to 3 weeks for Responders to therapy (those patients who achieved clinical remission at 3 weeks) were compared to the scores of Non-responders to therapy (those patients who did not achieve clinical remission at 3 weeks).

**Results:** All domain scores (social, emotional, systemic, and bowel) for Responders were statistically significantly better relative to Non-responders at 3 weeks (Fig. 1). Additional improvement in the IBDQ scores for each domain is observed for the Responders at 6 weeks ( $P < 0.005$ ).[figure1]



**Conclusion:** These results indicate that an early time to clinical remission is significantly associated with improvement in patient well-being, as measured by changes in IBDQ scores.

943

#### Rapid Symptom Resolution with Delayed Release Mesalamine in Mildly and Moderately Active UC

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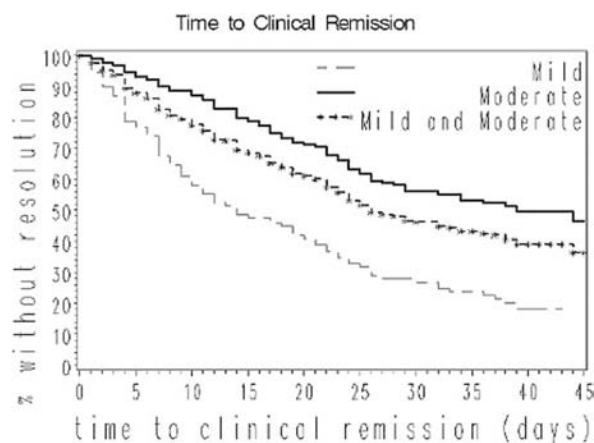
**Purpose:** To evaluate time to clinical remission in patients with mild and moderate active UC receiving 2.4 g/d of Asacol (mesalamine) delayed-release tablets.

**Methods:** Data from 2 multi-center, randomized, double-blind, active-controlled, 6-wk studies of similar design (ASCEND I&II) were combined and analyzed. The studies included patients with mild (PGA = 1) and moderate (PGA = 2) active UC. This analysis includes data from the 2.4 g/d active control arms of these studies. Clinical remission was defined as resolution (score = 0) of both rectal bleeding (RB) and stool frequency (SF). Resolution of RB was defined as the absence of visible blood in stools and resolution of SF was defined as a patient's return to his/her normal number of stools/day. To be included in analysis patients had to have symptoms at baseline. Time to clinical remission was defined as the first day of 3 consecutive days of complete symptom resolution based on symptoms recorded by patients daily through an integrated voice response system (IVRS).

**Results:** 687 patients were randomized in the 2 studies, of which 349 received 2.4 g/d. Based on IVRS data, the median time to clinical remission in patients with mild and moderate active UC was 26 days (95% CI 24,33). Time to clinical remission by disease severity is shown below:[figure1] In addition, results of the time to complete resolution analysis by individual symptoms and disease severity are shown below:

	Mild and Moderate UC (Median)	Mild UC (Median)	Moderate UC (Median)
RB	15 days (95% CI, 10,18)	4 days (95% CI, 3,5)	21 days (95% CI, 17,28)
SF	21 days (95% CI, 16,24)	10 days (95% CI, 7,15)	26 days (95% CI, 22,38)





Asacol 2.4 g/d was well-tolerated, with adverse events consistent with those described in the current prescribing information. In pivotal clinical studies of active UC, the most frequent adverse events reported for Asacol were headache, abdominal pain, and eructation.

**Conclusion:** In active UC, rapid symptom relief is a key treatment goal. Asacol 2.4 g/d provided rapid symptom relief in patients with mild and moderate active UC.

944

#### Comparable Pharmacokinetics (PK) of Two Delayed Release Formulations of Oral Mesalamine

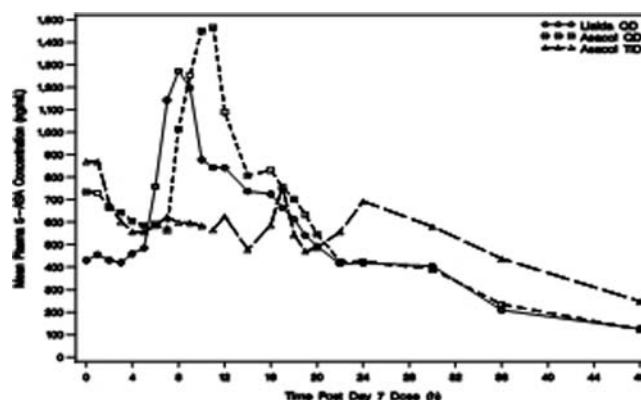
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**Purpose:** Both Asacol® and Lialda™ are delayed release mesalamine preparations for topical action in the colon with a pH dependent coating that controls mesalamine release at pH  $\geq 7$ . Lialda also contains lipophilic and hydrophilic excipients. According to labeling, Asacol is dosed TID and Lialda is dosed QD for mild to moderate active UC. The purpose of this study is to evaluate the PK parameters from 2.4 g/d of oral mesalamine administered as Lialda QD, Asacol QD and Asacol TID.

**Methods:** 37 healthy volunteers completed the randomized, open-label, parallel group, steady state PK study. All doses were taken within 30 minutes of a meal/snack, and subjects were dosed for 7 consecutive days. Plasma samples were obtained once daily up to day 7 and for 48 hrs after the first dose on day 7. Urine was collected over 8 hr intervals for 24 hrs after the first dose on day 7. Plasma and urine samples were analyzed for 5-ASA & N-Ac-5-ASA using a validated LC/MS assay. PK parameters were calculated using non-compartmental methods.

**Results:** 5-ASA plasma PK parameters and profile of all 3 treatment arms are shown in the following Table and Figure:

[figure1]The plasma PK parameters for 5-ASA & N-Ac-5-ASA were comparable across all treatment arms. The total (5-ASA & N-Ac-5-ASA) urinary excretion was 18%, 17.7%, and 15.2% for Lialda QD, Asacol QD, and Asacol TID, respectively.



**Conclusion:** Overall, Asacol and Lialda dosed QD exhibited a similar PK profile in healthy volunteers. These results suggest no apparent differences in the release profile of Lialda or Asacol given once daily. In addition, although not statistically significant, the Asacol TID arm shows less fluctuation relative to the Lialda QD arm ( $P = 0.56$ ); clinical significance unknown.

945

#### Previous History of Steroid Use Does Not Preclude Treatment with Mesalamine in Ulcerative Colitis (UC)

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**Purpose:** To determine effect of high dose delayed-release oral mesalamine (4.8 g/d) in patients with moderately active UC previously treated with oral or IV steroids.

**Methods:** Data from 2 multi-center, randomized, double-blind, active-controlled studies of similar design (ASCEND I&II) were combined and analyzed. Efficacy and safety of delayed-release mesalamine 4.8 g/d (investigational 800 mg tab) was compared with 2.4 g/d (Asacol, marketed 400 mg tab) for treatment of mildly and moderately active UC. The primary efficacy variable in the combined analysis was treatment success in patients with moderately active UC (defined as baseline Physician's Global Assessment [PGA] score = 2). Treatment success was defined as improvement from baseline at week 6 in PGA accompanied by improvement in at least one clinical assessment (stool frequency, rectal bleeding, patient functional assessment [PFA], or sigmoidoscopy findings) and no worsening in any of the remaining clinical assessments. Improvement was defined as a decrease from baseline of at least 1 point based on a 4-point scale (0–3). Improvement in the individual clinical assessments was also assessed.

**Results:** A total of 423 analyzable patients with moderate UC were randomized in the 2 studies, of which 137 patients had received previous oral or IV steroid therapy. The incremental benefit of 4.8 g/d over 2.4 g/d was apparent in patients previously treated with steroids:

5-ASA Day 7 PK Parameters – Least Square Geometric Means (95% CI)

	Lialda QD	Asacol QD	Asacol TID
AUC <sub>24</sub> ng.hr/mL	13556 (7616,24128)	14358 (8132,25350)	10679 (6168,18491)
C <sub>max</sub> ng/mL	1553 (857,2812)	1420 (790,2550)	1145 (651,2016)
t <sub>1/2</sub> (hrs)	10.2 (5.8,17.9)	9.6 (5.6,16.5)	8.5 (5.0,14.7)
Fluctuation Index(%)	240 (163,352)	182 (125,266)	206 (143,297)

Treatment Success at Week 6 in Moderate UC Patients

	2.4 g/d (N = 223)	4.8 g/d (N = 200)
Previous Steroid Users	52%	79%*

\* $P < 0.01$  stratified by protocol using CMH test

Improvement in the individual clinical assessments further support the response of 4.8 g/d in patients previously treated with steroids:

Improvement at Week 6 In Moderate UC Patients Previously Treated with Steroids

	2.4 g/d (N = 75)	4.8 g/d (N = 62)
PGA	72%	91%*
Stool Frequency	64%	80%
Rectal Bleeding	66%	89%*
Sigmoidoscopy	65%	82%*

\* $P < 0.05$  stratified by protocol using CMH test

The 4.8 g/d dose of mesalamine was well tolerated, with adverse events comparable to 2.4 g/d.

**Conclusion:** A previous history of steroid use does not preclude treatment with mesalamine. There is a role for mesalamine in moderate UC patients previously treated with steroids. UC patients with moderately active disease previously treated with oral or IV steroids respond better to higher initial doses (4.8 g/d) of mesalamine.

## 946

### Authorship and Industry Sponsorship in Treatment Trials in Inflammatory Bowel Disease

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**Purpose:** The International Committee of Medical Journal Editors (ICMJE) criteria for authorship may not be uniformly applied. Purpose: To examine the relationship between the funding source, authorship, and journal impact factor of published therapeutic trials in IBD.

**Methods:** Prospective drug and device treatment trials for IBD published in English between April 1, 2005 and March 31, 2007 were identified on PubMed. The source of funding, journal name and ISI impact factor, affiliation of authors, disease studied, study design and outcome, statements of conflict of interest (COI), and acknowledgement of non-author writers were recorded.

**Results:** Seventy-four studies were published in 18 medical journals: 52 (70%) were multi-center and 50 (68%) did not have U.S. authors. There were 32 Crohn's disease studies, 27 ulcerative colitis studies, and 5 of both. There were 43 (58%) industry-sponsored studies, 13 (18%) studies sponsored by governments or foundations, and in 18 (24%) the funding source was not stated. Industry studies were more commonly randomized controlled trials (86%) than non-industry studies (42%). The experimental treatment effect was positive in 63 (85%) trials and negative in 11, and 9 of the 11 negative trials were industry-sponsored. The median impact factors for the journals in which positive and negative studies were published was the same, 3.43,  $P = 0.774$ . The median impact factor for the journals in which industry sponsored studies were published was 3.43, the same as for non-industry studies. The median impact factor was higher (7.69 vs. 3.01,  $P = 0.001$ ) for the 35 trials with COI statements compared to the 39 without statements. There was no significance difference in the median impact factors (5.12 vs. 3.01,  $P = 0.11$ ) of journals for the 30 industry-sponsored studies with industry employee authors compared to the 13 industry-sponsored studies without employee authors. Non-author professional writers were acknowledged in 23% of industry studies.

**Conclusion:** The majority of treatments trials in IBD are Industry sponsored, and most industry studies have industry employee co-authors. IBD treatment studies with COI statements are published in journals with higher impact factors. The median impact factors for journals that published positive compared to negative studies was the same. Nearly a fourth of IBD treatment trials do not identify the funding source. Differences may be due to lack of uniformity in use of the ICMJE criteria for authorship and non-uniform journal guidelines for publication.

## 947

### Isolated Gastroduodenal Crohn's Disease Presenting with Acute Pancreatitis

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**Purpose:** Gastroduodenal Crohn's disease (GCD) occurs in 0.5–4% of patients with ileocolonic disease, but very rarely does it occur as an isolated identity and according to various studies is frequently difficult to treat with medical and surgical interventions. In addition acute pancreatitis has occasionally been associated with Crohn's disease, but the exact etiology remains unclear. We present a patient with multiple episodes of acute pancreatitis, nausea, vomiting, and weight loss who was found to have gastric granulomas on EGD and was treated with medical therapy.

**Methods:** We present a case of a 50-year-old male with no past medical history who initially presented to the out-pt GI clinic with the history of a recent episode of pancreatitis 2 months prior, where the patient had complaints of nausea, vomiting, and a 15 pound wt loss. At this presentation the patients' lipase was 1195 and amylase was 187. An EGD was done which showed severe acute and chronic erosive gastritis, with focal tendency toward superficial aphthous ulcers, focal microgranulomas, with no evidence of malignancy or H. Pylori. A colonoscopy showed no endoscopic evidence of Crohn's disease in the ileum or colon or any bleeding. Our patient was started on prednisone taper, mesalamine, and prilosec after which improved significantly even though there was no evidence of ileal of colon involvement. Prednisone was tapered down to 5 mg/day and he developed vomiting and weight loss. Our patient was taken off mesalamine and was placed on 6-MP 100 mg daily.

**Results:** The patient has been continued on 6-MP for more than 7 years now and his gastroduodenal crohn's disease has remained clinically asymptomatic.

**Conclusion:** Isolated GCD is rare; this is demonstrated by the fact that only 1 of 940 Crohn's patients from a major Dutch university referral center had isolated proximal CD and that the largest series ever published of isolated GCD comprised only 7 patients. Granulomas on biopsy in isolated GCD is an even rarer finding. In a series of 49 patients with CD and gastroduodenal involvement, more than 75% of the patients showed abnormal gastroduodenal biopsies, only 9% of patients had granulomas. Also worth noting is that when CD does involve the upper gastrointestinal tract, there is nearly always concomitant disease in the small bowel or colon, to which there is no evidence in our patient. The association of the GCD presenting with acute pancreatitis is a rare occurrence. And our patient was treated with 6-MP and had good response.

## 948

### Transplantation of Human Cord Blood Mononuclear Cells on Reversion of Experimental Inflammatory Bowel Disease

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**Purpose:** Inflammatory bowel disease (IBD) is a chronic intestinal inflammation, including Crohn's disease and ulcerative colitis, with epithelial injury. Many different reagents have been tried in last decade but there is still no effective therapy. Recently, stem cell transplantation (SCT) has been studied as therapy for IBD. Although accumulating data indicate that SCT may serve as a very promising approach, the mechanisms of how it works are still largely unknown and the limitation of auto-BMHSCT and mobilized PBHSCT makes it difficult to generalize these therapies. Cord blood is easy to get and could be an ideal resource of donor cells for SCT. In this study, we investigate the effects of transplantation of cord blood cells on experimental IBD and its mechanism.

**Methods:** To induce colitis in mice, CD4+CD25- T cells were isolated by magnetic separation from spleen of Balb/c mice and transferred into Balb/c.SCID mice i.p. The recipient mice were then administrated i.v. with human CBMNs or with saline as control. To determine whether hCBMNs are present in intestinal tissues of the recipient mice, hCBMNs were labeled with CM-Dil prior to transfer. The mice were sacrificed five weeks later and the various tissues were removed and processed for paraffin-embedded sections.

**Results:** Three to five weeks after first cell transfer, the recipient mice developed intestinal inflammation with characterization of colitis similar to human patients. The lesions in the mice treated with hCBMNs were improved than that of control mice. Four weeks later after second transplantation, many CM-Dil+ hCBMN-derived cells were distributed in intestinal mucosa and submucosa of the recipient mice, indicating that hCBMN-derived cells were involved in regeneration of the colon.

**Conclusion:** Put all together, our data indicated that systemically administrated hCBMNs responded to an adequate tissue lesion and resulted in accelerated tissue repair in mouse IBD. hCBMNs could be potentially used as therapy of the patients with IBD.

## 949

#### Crohn's Disease Diagnosed by Capsule Endoscopy in Patients with Obscure Gastrointestinal Bleeding

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**Purpose:** The purpose of this study is to describe and compare cases of Crohn's disease diagnosed by capsule endoscopy performed for the evaluation of obscure gastrointestinal bleeding.

**Methods:** We retrospectively reviewed the records of all patients who underwent Video Capsule Endoscopy at Wake Forest University Baptist Medical Center from January 2004 to September 2006 for the evaluation of obscure gastrointestinal bleeding. All patients had overt or occult bleeding unexplained by findings on colonoscopy, upper endoscopy, or other imaging modality. We then identified all patients with small bowel ulceration suspicious for Crohn's disease and collected relevant data from the medical records. Patients with small bowel erosions not felt to be due to Crohn's disease were not included.

**Results:** From a total of 238 capsule endoscopies performed, 198 studies were for the evaluation of obscure gastrointestinal bleeding. Six patients (3%) were identified with small bowel ulceration suspicious for Crohn's disease. Five of the six patients were not taking NSAIDs at the time of the examination. 83.33% of the six patients had a positive IBD serology (Prometheus Labs, San Diego, CA). Mean age was 35 years and four were females (66%). All six patients diagnosed with Crohn's Disease by capsule endoscopy were being evaluated for iron deficiency anemia requiring multiple blood transfusions. Only two patients had mild symptoms of abdominal pain and diarrhea. The duration of anemia to diagnosis was from 11 months to 15 years. The mean follow up of these six patients was 14 months. Subsequent therapy included iron supplementation for all patients. Mesalamine was initiated in 5 patients and budesonide in one. Two patients subsequently required immunomodulators and another began infliximab, however none required surgery.

**Conclusion:** Crohn's disease can present with obscure gastrointestinal bleeding with or without typical symptoms of abdominal pain and diarrhea. At our medical center, we found that 3% of patients being evaluated for obscure GI bleeding by capsule endoscopy had Crohn's disease isolated to the small bowel. Of these patients, 66.67% were young females. These cases can generally be managed medically and may represent a subset of patients with mild disease.

## 950

#### High Rates of Vitamin D Deficiency and Osteopenia in Crohn's Disease Are Associated with Abnormal Absorption of Oral Vitamin D

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**Purpose:** Crohn's disease (CD) patients have high rates of vitamin D deficiency that may result in poor bone mineral density (BMD). However, the causes of vitamin D deficiency in CD are unclear. As vitamin D is absorbed in the small bowel, it has been proposed that CD patients cannot absorb vitamin D adequately. The aims of this study were to assess vitamin D nutritional status, vitamin D intestinal absorption capacity, and BMD in CD patients.

**Methods:** 21 consecutive adult patients with CD presenting for routine office visits to Boston Medical Center were enrolled from January 2007 to April 2007. In addition to demographic and clinical factors, baseline serum levels of 25(OH)D, an indicator of vitamin D nutritional status, were measured. To assess vitamin D absorption, patients ingested 50,000 IU of vitamin D<sub>2</sub>. Serum vitamin D<sub>2</sub> levels were measured via HPLC 12 hours later. Vitamin D deficiency was defined as serum 25(OH)D levels of  $\leq 20$  ng/ml. A change in the serum D<sub>2</sub> level of  $\geq 50$  ng/ml 12 hours after ingestion of 50,000 IU of vitamin D<sub>2</sub> was considered normal absorption (Holick et al, Am J Nutr 1985). Bone density scans of hip and spine were also obtained.

**Results:** This cohort was young (mean age  $44 \pm 14$  y), predominantly without active disease (by CDAI, ESR, CRP), and well nourished (by albumin, Hct) and may not routinely be screened for vitamin D deficiency or osteopenia. Of the 21 CD patients that completed baseline and absorption testing, 61% (13/21) were vitamin D deficient ( $14.2 \pm 3.7$  ng/ml). 85% (11/13) of patients with vitamin D deficiency showed evidence of vitamin D malabsorption ( $34.3 \pm 12$  ng/ml). Of the 18 patients who underwent bone density scans, 56% (10/18) were found to have osteopenia (N = 8) or osteoporosis (N = 2) as defined by the WHO classification. 70% (7/10) of patients with low BMD were vitamin D deficient and 86% (6/7) had abnormal absorption of vitamin D. Among the 10 low BMD patients, two were on corticosteroids and one is a smoker.

**Conclusion:** Patients with CD have high rates of vitamin D deficiency and reduced BMD which may be associated with abnormal absorption of vitamin D.

## 951

#### Absence of NOD2 Polymorphisms in Crohn's Disease Patients with Uveitis

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**Purpose:** NOD2 (also called CARD15) mutations have been found to cause a rare autosomal dominant form of uveitis called Blau syndrome (BS). Polymorphisms in NOD2 distinct from those found in BS predispose

individuals to Crohn's disease (CD). Previous studies suggest the presence of specific NOD2 polymorphisms may have an effect on the presentation of extraintestinal manifestations of CD, such as uveitis. It was hypothesized that NOD2 polymorphisms influence the presence of uveitis in a CD population.

**Methods:** Uveitis patients diagnosed with CD seen at the Casey Eye Institute Uveitis Clinic and CD patients with no ocular involvement seen at the Gastroenterology Clinic at Oregon Health and Science University were recruited into the study. All 12 exons of NOD2 were genotyped either by direct sequencing or by denaturing high performance liquid chromatography. Statistical analyses were performed using Fisher's Exact Test to compare the frequency of NOD2 CD specific polymorphisms in CD patients with versus without uveitis.

**Results:** A total of 37 CD patients were genotyped: ten patients (seven female, three male) with uveitis related to CD, and the other 27 with no ocular involvement (18 female, nine male). All patients were Caucasian, including one Hispanic, one African American/Caucasian, and two patients with mixed Caucasian and Native American ancestry. The group with uveitis was older (mean age 48, range 35–79) compared to the patients without uveitis (mean age 38, range 19–70). Of the 10 patients with both CD and uveitis, seven had colitis and three had ileocolitis. Among the 27 CD patients without uveitis, there were 12 with ileitis, seven with ileocolitis, and eight with colitis alone. The three most common NOD2 polymorphisms (corresponding to amino acid changes R702W, G908R and 1007fs) were identified in 12 of the 27 patients without uveitis (at a combined allele frequency of 32%) but were absent in the 10 patients with uveitis. This difference, 32% versus 0%, was statistically significant with a  $p$ -value = 0.015.

**Conclusion:** Mutations in NOD2 that contribute to the genetic predisposition of CD are absent from the subset of CD patients who develop uveitis. This absence is consistent with the colitis phenotype observed in the uveitis cohort compared to CD patients with no ocular involvement.

## 952

### Efficacy and Safety of Rifaximin as Maintenance Therapy for Mild-Moderate Crohn's Disease Refractory to Multiple Medical Therapies

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**Purpose:** Rifaximin is a nonabsorbable antibiotic with broad-spectrum activity against intestinal pathogens. Previous studies, including our report of clinical improvement with rifaximin in 55% of 55 patients with mild-moderate Crohn's disease (CD), have suggested benefits of rifaximin in CD. However, limited data are available on the efficacy of antibiotics for maintaining CD remission. This retrospective review evaluated rifaximin as maintenance therapy in patients with mild-moderate CD refractory to multiple medical therapies.

**Methods:** Medical records for patients who received open-label rifaximin for active mild-moderate CD refractory to prior therapies were reviewed. Those who exhibited clinical improvement during rifaximin treatment and continued rifaximin as maintenance therapy were included. Patients received 200 mg twice daily (b.i.d.), 200 mg three times daily, 400 mg b.i.d., or 600 mg b.i.d. Concomitant medications were permitted.

**Results:** The analysis included 28 patients (mean age 40 y) with a mean CD duration of 13 years; 14 had isolated ileitis, 10 had ileocolitis, and 4 had isolated colitis. Prior to initiation of rifaximin maintenance therapy, patients had been receiving a mean of 1.9 CD drugs per day. Concomitant medications during maintenance included aminosalicylates ( $N = 18$ ; 64%), ciprofloxacin or metronidazole ( $N = 11$ ; 39%), budesonide ( $N = 4$ ; 14%; mean dose 6.7 mg/d), prednisone ( $N = 3$ ; 11%; mean dose 15.3 mg/d), immunomodulators (6-mercaptopurine, azathioprine, or methotrexate;  $N = 9$ ; 32%), and infliximab ( $N = 3$ ; 11%). Mean dose of rifaximin during maintenance was 685 mg/d; 6 patients received 400 mg/d, 8 received 600 mg/d, 12 received 800 mg/d, and 2 received 1200 mg/d. Overall, patients maintained clinical improvement for a mean duration of 5.2 months (range, 3–23 months). Mean duration of response was similar for each disease location: 6.1 months for

patients with ileitis, 4.8 months for those with ileocolitis, and 7.8 months for those with colitis. Drug-related adverse events (AEs) were oral thrush ( $N = 1$ ) and nausea ( $N = 2$ ). No patients discontinued rifaximin therapy due to an AE.

**Conclusion:** In this open-label study, rifaximin (400–1200 mg/d) effectively and safely maintained clinical improvement for a mean duration of 5.2 months in patients with mild-moderate CD refractory to multiple therapies. Maintenance duration did not depend on disease location. Dose-ranging, placebo-controlled trials of rifaximin as maintenance therapy in CD are warranted.

## 953

### Adenocarcinoma in Ileal Pouch-Anal Anastomosis: The Cleveland Clinic Experience

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**Purpose:** Total proctocolectomy with ileal pouch-anal anastomosis substantially reduces the risk for dysplasia and cancer associated with ulcerative colitis (UC). Cancer in ileal pouch-anal anastomosis (IPAA) patients with underlying UC is a rare, which has only been reported as single cases. Natural history of IPAA cancer in these patients and its risk factors have not been investigated and there is lack of consensus for endoscopic cancer surveillance for these patients. The aim of the study was to characterize the natural history and clinical features, and histology in a group of patients with cancer of IPAA.

**Methods:** Pouch database of 2,750 cases was searched. All patients had a preoperative diagnosis of UC or indeterminate colitis. Patients with cancer from the pouch and/or anal transitional zone (ATZ) were identified. Clinical features of these patients were characterized.

**Results:** Eight patients (0.29%) with adenocarcinoma of the pouch and/or ATZ were identified from the database. Average age at cancer diagnosis was  $56.8 \pm 12.5$  (SD) years. The mean duration from IBD diagnosis to cancer and from ileostomy take-down after IPAA to cancer diagnosis was 22.8 and 8.7 years, respectively. Most [5/8(62.5%)] had regular pouch endoscopic surveillance after IPAA. Six cases had ATZ cancers and 2 had cancers of the pouch.

**Conclusion:** The risk for cancer of IPAA is small but real, which can occur in UC patients without pre-colectomy diagnosis of dysplasia or cancer. A disproportional high number of these patients had post-operative Crohn's disease of the pouch. The majority of the patients had histologic poorly-differentiated cancer. Mucosectomy does not necessarily prevent cancers of the ATZ or pouch.

#### Demographic and Clinical Features of the 8 Patients with Cancer of IPAA

	Cases	%
Proctocolectomy performed for dysplasia or cancer	3	42.8
Pancolitis	6	75.0
Family history of colon cancer	1	12.5
Staged pouch surgery	7	87.5
Hand-sewn anastomosis with mucosectomy	3	42.8
Crohn's disease of the pouch	4	50.0
Poorly differentiated cancer	5	62.5
Tumor metastasis at diagnosis	2	25.0

## 954

### Nutritional Changes in Crohn's Disease Patients Treated with Infliximab

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**Purpose:** To assess the nutritional changes, particularly enterocyte function and body composition that occurs in Crohn's disease patients beginning infliximab, we evaluated Crohn's disease patients immediately before infliximab administration and again after 6 weeks and 6 months of therapy.

**Methods:** Crohn's disease patients beginning infliximab for ileocolonic, non-fistulizing disease were entered. Assessment included parameters of: 1) Disease activity, such as Inflammatory Bowel Disease Questionnaire (IBDQ), 2) A combined index of inflammation and enterocyte function: Prognostic Inflammatory and Nutrition Index (PINI), 3) Enterocyte function, such as plasma folate and citrulline, and 4) Body composition, such as lean muscle mass (LMM) measured by DEXA scans, BMI, and resting energy expenditure (REE) measured by indirect calorimetry.

**Results:** The study enrolled 7 patients, 6 of whom had active inflammation characterized by CRP > 1.0 mg/dL. Most patients had an improvement in disease activity. All of the patients had a drop in their PINI after 6 weeks or 6 months of infliximab treatment (-3.35,  $P = 0.04$ ). Those with active inflammation at enrollment had a greater drop in PINI (-4.65,  $P = 0.03$ ). Plasma folate significantly increased after 6 months of infliximab therapy. There was an increase in BMI and LMM, but only the change in BMI was significant. Changes in citrulline and REE were inconsistent among subjects.

**Conclusion:** These findings suggest that Crohn's disease patients have improvements in both inflammation and nutrition (PINI) with infliximab therapy. An improvement in enterocyte function could account for the improved nutritional status. BMI increased significantly and was partly accounted for by an increase in LMM. Whether infliximab alters body composition or merely increases absorption is yet to be determined. These finding also support the use of PINI in Crohn's patients as an overall marker of inflammation and nutrition and possible measure of response to infliximab therapy.

Change in Nutritional Parameters after Infliximab Initiation

Variable	Change	P-value
IBDQ	+38.0	0.058
PINI	-3.35	0.044
Folate (ng/ml)	+2.14	0.046
Citrulline (umol/L)	-1.43	0.792
LMM (g)	+872.33	0.440
BMI	+2.21	0.034
REE (kcal/kg/day)	-0.64	0.423

## 955

### Crohn's Disease-Associated Colonic Dysplasia & Cancer: Lessons Learned from 93 Cases

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**Purpose:** Endoscopic surveillance is not always employed for patients with colonic Crohn's disease (CD). In addition, management of CD-associated colonic dysplasia or cancer, once detected, is debatable. The aims of the study were to characterize clinical, endoscopic, and histologic features & natural history of CD-associated dysplasia/cancer as a source of information for 1) surveillance recommendations; 2) risk factors for progression from dysplasia to cancer; & 3) surgical treatment.

**Methods:** Database search was performed for patients with CD-associated dysplasia/cancer during the last 30 years. Biopsies and surgical specimens were reviewed by an expert GI pathologist. Demographic, clinical, endoscopic and surgical variables were studied.

**Results:** 93 patients with CD-associated dysplasia/cancer were identified: 32 (34%) had dysplasia, 22 (24%) had dysplasia and cancer and 39 (42%) had cancer without dysplasia. High-grade dysplasia (HGD) was found in 49/93 (53%) [72% of the dysplasia group and 43% of the cancer group] and was multifocal in 27/49 (55%) [57% in dysplasia group, and 54% in cancer group]. Low-grade dysplasia (LGD) was found in 29/93 (31%) [59%

in dysplasia group, and 16.4% in cancer group] and was multifocal in 13/29 (45%) [47% in dysplasia group, and 40% in cancer group]. 18/61 (30%) of cancer patients had dysplasia found in at least 1 preoperative endoscopy. CD characteristics are shown in Table 1. Patients with dysplasia who were treated with 5-aminosalicylates (5ASA) at any time, were less likely to progress to cancer (OR 2.94, 95% CI 1.22-7.12  $P = 0.016$ ) than those without 5ASA treatment.

**Conclusion:** 1) Dysplasia in colonic CD often is multifocal; 2) Concurrent dysplasia was found in a substantial number of CD-associated colon cancers; and 3) 5ASA use may protect from progression of dysplasia to cancer. Our findings support routine endoscopic surveillance for colonic CD as in ulcerative colitis and chemoprevention with 5ASA. Colonic CD with dysplasia may require radical surgery due to the multifocal nature of dysplasia and the risk for future cancer.

Risk Factors for Dysplasia Progression to Cancer

	Dysplasia only	Cancer(+/-dysplasia)	P value
CD duration before dysplasia/cancer diagnosis	14.7 (0-46)	17 (0-63)	0.45
Pancolitis	27/32 (84.3%)	43/61 (70.5%)	0.21
5ASA treatment	21/32 (65.6%)	24/61 (39.3%)	0.016
Primary sclerosing cholangitis	5/32 (15.6%)	7/61 (11.4%)	0.45

## 956

### Biopsy Practices Following the Diagnosis of Neoplasia in Patients Undergoing Surveillance Colonoscopy in Ulcerative Colitis (UC)

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**Purpose:** Current guidelines recommend that a minimum of 32 biopsies (bxs) be taken at each surveillance colonoscopy (SC) to exclude dysplasia in patients with longstanding UC. Previous questionnaire and retrospective studies suggest that this target is not being met.

**Aim:** To determine whether endoscopists change their bx practices after the discovery of epithelial dysplasia.

**Methods:** The Mount Sinai UC-Dysplasia Surveillance Database is an IRB-approved project that contains clinical, endoscopic, and pathologic information on UC patients who have undergone 2 or more SCs between 1994 and 2006. To determine whether bx practices were influenced by previous SC findings, the number of specimens available for histopathologic review from each segment were tabulated according to the descriptions of the pathology lab technician for each separate jar submitted. The number of specimens for all jars was summed and constituted the bx number for each SC. Bx numbers from SCs without prior dysplasia were compared to bx numbers from SCs in patients with findings of indefinite for dysplasia (IND), low-grade dysplasia (LGD), or high-grade dysplasia (HGD). The number of colorectal cancers (CRCs) without previous IND, LGD, or HGD were tabulated. Comparisons were made using Student's t-test with  $P < .05$  significant.

**Results:** We identified 187 patients who met our stated criteria. Their average duration of disease was 17 years, and their average age at first SC was 48 years. Among the 1083 SCs for which bx number was calculated, 523 were exams with no prior dysplasia (NoD). 332 SCs took place after IND, 177 after LGD, and 51 after HGD. Bx numbers per SC were less than recommended in surveillance guidelines. However, for patients who had previous dysplasia, more bxs were taken during SCs (see Table). Breakthrough CRC without previous dysplasia occurred in 1 case.

**Conclusion:** While not meeting current recommendations, endoscopists typically altered their bx practice in response to abnormal findings. Breakthrough CRC after SCs in which all prior bxs were dysplasia-free was uncommon ( $N = 1$ ), suggesting that current SC practices as performed in routine practice are adequate for preventing the development of advanced pathology.

	# SCs	Bxs per SC	P-value
NoD	523	13.7 ± 5.8	—
IND (no prior LGD, HGD, CRC)	332	16.7 ± 6.8	<.001
LGD (no prior HGD, CRC)	177	17.4 ±	<.001
HGD (no prior CRC)	51	18.1 ± 6.8	<.001

## 957

### Enterocutaneous Fistula after Closure of Temporary Ileostomy, Incidence, Management and Outcome

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**Purpose:** Diverting ileostomy is commonly used for temporary fecal diversion protecting lower gastrointestinal anastomosis. One of the less reported serious complications is the formation of enterocutaneous fistula (ECF) at the ileostomy site after its closure. Choosing a surgical or medical approach may be a dilemma for the surgeon. The aim of this study is to evaluate ECF incidence, management and outcome.

**Methods:** All patients who had temporary ileostomy for primary diversion following pelvic surgery between 1983 and 2006 were reviewed from the institutional colorectal surgery databases. Cases of ECF were identified; and clinical information was extracted.

**Results:** Total of 4116 patients (3165 pelvic pouch, 951 colorectal cancer) received temporary ileostomy. Eleven patients with ECF at the ileostomy site were identified (0.27%). Ten were from ileal pouch patients, one from the cancer group. For these patients, the mean ileostomy duration was 115 days (12–302). The mean presentation time of the ECF was 15 days post ileostomy closure (range 3–53). Eight patients had ECF daily output >200 cc. 4 of 8 had output higher than 900 cc/day (range 950–3800). Nine of 10 patients had fistula closure following bowel rest, with/without parental nutrition. The average duration to closure following medical therapy was 31 days (range 9–79). The only patient with Crohn's disease in this series failed conservative therapy and required abdominal surgery for fistula closure.

**Conclusion:** Enterocutaneous fistula at old ileostomy site occurs rarely. Most ECF will resolve promptly with medical management.

## 958

### Is Laparotomy Warranted at the Closure of Temporary Ileostomy? A Review of 571 Patients with Bowel Obstruction Following Restorative Proctocolectomy with Ileal Pouch

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**Purpose:** Small bowel obstruction (SBO) is a usual complication following major abdominal surgery, which frequently requires surgical intervention. Temporary ileostomy is commonly employed for fecal diversion, which requires a second surgery, albeit small, for closure. At the time of ileostomy takedown, instead of a local excision, would a full laparotomy be beneficial in reducing the risk of recurrent bowel obstruction?

**Methods:** Patients with SBO were identified from the institutional ileal pouch anal anastomosis (IPAA) database of 3176 cases during a 23-year period. Clinical details reviewed and analyzed included timing of ileostomy closure and incisions used.

**Results:** 794 episodes of SBO from 571 patients were identified following IPAA. Surgical intervention was required in 229 episodes (29%). Seventy six patients were excluded because no ileostomy was utilized (49), or ileostomy not closed (3) or closed at another institution. For the remaining 495 patients, average ileostomy duration was 120 days. The study group numbered 140 patients who had 1st episode of SBO before ileostomy closure. Depending on the incision type at the ileostomy takedown, the study group was divided into three subgroups: A) peristomal incision at the regular time of ileostomy takedown (> 7 wks), 102 patients; B) laparotomy at the regular time of takedown, 15 patients; C) laparotomy before the regular time of takedown, 23 patients. SBO recurrence was lower in patients who underwent a laparotomy (23.7%) than those who had peristomal incision (30.4%).

There were 130 patients (26.2%) who developed their 1st SBO within 60 days following ileostomy closure. Of these, 101 (77.7%) had only one episode of SBO. 80 of the 101 (80%) patients were managed medically without recurrence.

**Conclusion:** The ileostomy take down presents a valuable opportunity for patients who already display signs of obstruction. Laparotomy with full exploration at this point can safely reduce the risk of future bowel obstruction. The majority of bowel obstruction cases occurring immediately following take down can be successfully managed medically without recurrence.

#### Small Bowel Obstruction Recurrence after Ileostomy Takedown

	A	B	C	All laparotomy (B+C)
Number of patients	102	15	23	38
SBO Recurrence	31	4	5	9
Recurrent Rate	30.4%	26.7%	21.7%	23.7%
P value	—	NS	NS	NS
Recurrence require surgery	15	1	4	5
Re-op rate	14.7%	6.7%	17.4%	13.2%

SBO: small bowel obstruction.

#### Enterocutaneous Fistula at Old Ileostomy Site

Patient	Age/ Gender	Diagnosis	Ileostomy Duration	Closure Type	Time to Fistula Presentation (days)	Daily Output	Fistula Duration (days)
1	57/M	Ulcerative Colitis	114	Hand sewn	3	1000 cc	33
2	69/M	Ulcerative Colitis	98	Stapled	6	950 cc	OR closure
3	48/F	Ulcerative Colitis	12	Hand sewn	7	60 cc	9
4	40/M	Indeterminate Colitis	137	Stapled	53	40 cc	9
5	49/M	Indeterminate Colitis	109	Hand sewn	4	450 cc	12
6	63/M	Ulcerative Colitis	141	Hand sewn	28	225 cc	16
7	47/M	Ulcerative Colitis	83	Hand sewn	7	1525 cc	79
8	54/M	Indeterminate Colitis	92	N/A	12	3800 cc	47
9	34/M	Crohn's Disease	89	Hand sewn	6	200 cc	OR
10	44/F	Ulcerative Colitis	94	Hand sewn	34	30 cc	38
11	52/F	Colon Cancer	302	Hand sewn	9	450 cc	32

### Severe Crohn's Disease Symptoms Are Relieved by Certolizumab Pegol

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**Purpose:** Certolizumab pegol (CZP) is the first Fc-free PEGylated anti-TNF Fab' fragment. Lack of an Fc portion potentially avoids side effects.<sup>1</sup> The efficacy and safety of subcutaneous CZP 400 mg in patients (pts) with active Crohn's disease (CD) was shown in a large Phase III trial (PRECiSE 2).<sup>2</sup> There were significant improvements in all domains of the Inflammatory Bowel Disease Questionnaire (IBDQ).<sup>3</sup> The present analysis of PRECiSE 2 IBDQ results by item and domain is presented to describe the ability of CZP to relieve symptoms frequently reported by pts as severe.

**Methods:** In PRECiSE 2, a 26-week (wk) double-blind study, pts with a clinical response at Wk 6 following induction therapy with CZP were randomized to CZP (N = 215) or placebo (PBO, N = 210) every 4 wks up to Wk 24. Pts completed the IBDQ<sup>4</sup> at Wks 0, 6, 16, and 26. The proportion of pts reporting severe or extremely severe impact was calculated at baseline for each IBDQ item. Analysis of covariance was used to compare IBDQ item scores at Wk 26 between groups.

**Results:** At baseline, 35–62% of pts reported the following CD symptoms as severe: loose bowel movements; abdominal cramps; abdominal pain; fatigue; lacking energy; sleep problems; not feeling relaxed; and feeling generally unwell. By Wk 26, all these items were significantly improved in the CZP group compared with PBO ( $P \leq 0.042$ ). Emotional problems were also less common in the CZP group at Wk 26 than in the PBO group: feeling frustrated ( $P = 0.006$ ), afraid of not finding a washroom ( $P = 0.013$ ), feeling depressed ( $P = 0.008$ ), worried ( $P = 0.047$ ), embarrassed ( $P = 0.007$ ) or irritable ( $P = 0.024$ ), and feeling a lack of understanding from others ( $P = 0.003$ ). Compared with PBO, pts receiving CZP were less inclined to delay or cancel a social engagement because of bowel problems ( $P = 0.022$ ).

**Conclusion:** CZP improved the majority of CD symptoms, including those that were frequently reported by pts as being severe. Several bowel and systemic symptoms were significantly improved by CZP maintenance treatment, as measured by the IBDQ. CZP treatment also relieved the burden of CD on emotional and social aspects of pts' lives.

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### Sustained Efficacy and Tolerability of Certolizumab Pegol over 18 Months: Data from PRECiSE 2 and Its Extension Studies (PRECiSE 3 and 4)

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**Purpose:** Certolizumab pegol (CZP), a PEGylated Fc-free Fab' anti-TNF, was effective and well tolerated in a 26-week (wk) open-label induction, double-blind maintenance trial in active Crohn's disease (CD; PRECiSE 2 [P2]).<sup>1</sup> Patients (pts) could enter open-label extension studies evaluating long-term continued maintenance of response (PRECiSE 3 [P3]) or re-induction and maintenance after relapse (PRECiSE 4 [P4]). P3 and P4 are ongoing studies; results after 12 and 18 months' treatment are given here.

**Methods:** P2 pts with a clinical response to CZP 400 mg induction (Wks 0, 2, and 4) at Wk 6 (64.1%) were randomized to CZP 400 mg (N = 215) or placebo (PBO; N = 210) every 4 wks Wk 8–24. Pts who completed P2 and entered P3 received 4-weekly CZP 400 mg for up to 5 years. Pts who relapsed (CD Activity Index [CAI] increase  $\geq 70$  or CAI  $\geq 350$ ) after randomization in P2 and entered P4 received re-induction with CZP 400 mg (Wks 0, 2, 4) then maintenance dosing every 4 wks, ie, re-induction from P2 into P4 was a single dose. In P3 and P4, efficacy was assessed by the Harvey–Bradshaw Index (HBI: remission = HBI score  $\leq 4$ ; response = HBI decrease  $\geq 3$ ).<sup>2</sup> Pts lost to follow-up or withdrawn were treated as nonresponders. Adverse events were monitored.

**Results:** Remission at the end of P2 (Wk 26) was achieved by 47.9% (CAI) and 48.4% (HBI) of pts receiving CZP (N = 215). Of these, 41.9% (N = 90) and 37.2% (N = 80) were in remission after 12 and 18 months, respectively, of continued treatment in P3. Of pts re-induced with CZP in P4, 29% (N = 14) achieved remission. The remission rate was stable (35% at Month 6 and 12 [N = 17] of P4). Among pts from the P2 PBO group re-induced with CZP, 44% achieved remission. Remission rates were 44% (Month 6) and 36% (Month 12). Re-exposure of P2 PBO pts to CZP raised no safety concerns.

**Conclusion:** Sustained long-term efficacy was observed with CZP in the treatment of CD. Re-induction with a single supplemental dose of CZP 400 mg after loss of response was a well-tolerated, successful therapeutic strategy.

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### A Comprehensive Evaluation of the Impact of Crohn's Disease and Its Treatment on Patients Is Achieved Using a Combination of the CAI and IBDQ

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**Purpose:** Diarrhea, abdominal pain, and weight loss are common symptoms of Crohn's disease (CD); the most commonly used measure for these symptoms is the CD Activity Index (CAI). CD also greatly impacts patients' physical, emotional, and social functioning.<sup>1</sup> These aspects are measured using the Inflammatory Bowel Disease Questionnaire (IBDQ).<sup>2</sup> This analysis compared and contrasted CAI and IBDQ information using data from PRECiSE 2.

**Methods:** In PRECiSE 2, patients with a clinical response at Wk 6 following induction with certolizumab pegol (CZP) were randomized to CZP (N = 215) or placebo (PBO; N = 210) every 4 wks up to Wk 24.<sup>3</sup> CAI and IBDQ data were collected at Wks 0, 6, 16, and 26. Correlations were evaluated at Wk 26, or at baseline, using Pearson's correlation for CAI total score and IBDQ total or domain scores, and Spearman's rank correlation for CAI and IBDQ items scores. Missing data were not imputed. Correlation coefficients (R) were termed moderate ( $\geq 0.3$ ) or high ( $\geq 0.5$ ).<sup>4</sup>

**Results:** CAI and IBDQ total scores correlated moderately at baseline ( $R = -0.344$ ; N = 255) and highly at Wk 26 ( $R = -0.603$ ). CAI total score (N = 255) correlated more with the bowel ( $R = -0.593$ ) and systemic ( $R = -0.566$ ) symptom domains of IBDQ than with the IBDQ emotional ( $R = -0.517$ ) and social ( $R = -0.469$ ) function domains. Abdominal pain, diarrhea, and general well-being, assessed in both measures, were highly correlated ( $R = -0.610$  to  $-0.721$ ; N = 244). Weakly correlated items ( $R < 0.3$ ) included CAI clinical objective measures (taking medication for diarrhea, abdominal mass, hematocrit, and low body weight) and some IBDQ emotional and social function items (passing gas, rectal bleeding, accidental soiling, weight problems, and lack of understanding from others).

**Conclusion:** The CAI and IBDQ assess interrelated but nonidentical aspects of CD. The CAI reflects physical more than emotional or social

aspects, while the IBDQ covers all aspects but is less comprehensive than the CDAI for clinical objective measures. Both instruments in combination provide a comprehensive evaluation of the impact of CD and its treatment.

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### Minimally Important Difference for WPAI:CD Scores: Defining Relevant Impact on Work Productivity in Active Crohn's Disease

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**Purpose:** Crohn's disease (CD) causes significant economic burden, especially productivity losses.<sup>1</sup> Certolizumab pegol, a PEGylated Fc-free Fab' is effective in CD (PRECiSE trials<sup>2,3</sup>). Clinical response (CD Activity Index [CDAI]) was associated with improved health-related quality of life (Inflammatory Bowel Disease Questionnaire [IBDQ]) and increased productivity (Work Productivity and Activity Impairment questionnaire [WPAI:CD]).<sup>4</sup> We estimated the smallest changes in WPAI:CD scores in PRECiSE 1 perceived as beneficial by patients/clinicians — minimally important difference (MID).

**Methods:** Using an anchor-based method (relationship between WPAI:CD and independent measures), regressions compared changes in WPAI:CD with those for CDAI and IBDQ between Weeks 0 and 26. Known meaningful changes in CDAI (50 points) and IBDQ (16 points) were used to derive 2 MID estimates. Using a distribution-based method, 3 MID estimates were derived from small (0.2) to moderate (0.5) effect sizes (ES, magnitude of change in WPAI:CD /variability in baseline scores). The 5 MID estimates gave the first MID assessment in WPAI:CD.

**Results:** IBDQ correlated more closely than CDAI with WPAI:CD (Spearman coefficients 0.44–0.65 vs 0.35–0.52); CDAI yielded the lowest MID values. A moderate ES of 0.5 gave outlying values. Mean MID estimates were 6.5% (absenteeism), 6.1% (presenteeism), 7.3% (overall work impairment) and 8.5% (activity impairment) (Table).

**Conclusion:** MID provides a useful benchmark to interpret treatment outcome beyond statistical significance. Changes in WPAI:CD scores >7% can be regarded as sizable changes in workplace productivity.

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### Comparison of the Penetration of Certolizumab Pegol and Adalimumab in Inflamed and Noninflamed Mouse Tissue

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**Purpose:** PEGylated molecules diffuse relatively slowly out of the blood. The disposition of such molecules may therefore alter during inflammation. Certolizumab pegol is an Fc-free PEGylated Fab' of a humanized anti-TNF $\alpha$  monoclonal antibody. The attachment of polyethylene glycol (PEG) increases its tissue bioavailability to a level equivalent to or greater than that of conventional anti-TNFs such as adalimumab. This study compared the in vivo disposition of certolizumab pegol and adalimumab in noninflamed and inflamed mouse tissue using a novel noninvasive biofluorescence method.

**Methods:** Certolizumab pegol and adalimumab, labeled with the low-molecular weight dye Alexa 680, were administered separately by intravenous injection (2 mg/kg) to naïve DBA/1 mice and to DBA/1 mice with ongoing collagen-induced arthritis. Drug accumulation was measured in the hind paws at multiple time points up to 26 hours using a Xenogen IVIS200 biofluorescence imager. ELISA was used to assay for drug serum levels in tail blood samples.

**Results:** The penetration of both agents was higher into inflamed tissue than into noninflamed tissue. Certolizumab pegol penetrated more effectively into inflamed arthritic paws than adalimumab: the maximum inflamed:noninflamed tissue ratio achieved by certolizumab pegol was 3.9:1 (at 6 hours post-administration) compared with 1.9:1 (at 3 hours) for adalimumab. Certolizumab pegol had an elimination half-life in inflamed tissue of 27.8 hours; the corresponding value for adalimumab was 5.5 hours.

**Conclusion:** Certolizumab pegol displayed higher and more prolonged exposure in inflamed tissue than adalimumab in this animal model. Certolizumab pegol, unlike adalimumab, appears to readily enter edematous inflamed tissue, while sparing noninflamed tissue. This is a property that may be conferred by PEGylation. Adalimumab's short period of exposure in the inflamed tissue is possibly because it is readily recycled out of the tissue by the FcRn receptor. In comparison certolizumab pegol has a prolonged exposure because it is Fc free and cannot be recycled by the same mechanism. In the treatment of inflammatory disorders such as Crohn's disease, increased drug exposure at the site of inflammation might be an important consideration.

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### Measurement of Urinary Excretion of 40 kDa Polyethylene Glycol (PEG) after Subcutaneous Administration of Certolizumab Pegol in Rats

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**Purpose:** Certolizumab pegol, an Fc-free PEGylated Fab', binds human tumor necrosis factor (TNF)  $\alpha$  with high affinity. The PEG component of certolizumab pegol comprises two 20 kDa chains of PEG-monomethyl ether attached covalently and site-specifically to a hinge thiol on the Fab'. Hemodynamic properties of proteins are altered by PEGylation, leading to

WPAI:CD scores	MID Estimate (%)				
	$\Delta$ CDAI 50*	$\Delta$ IBDQ 16*	ES = 0.2	ES = 0.3	ES = 0.5
Absenteeism (N = 321)	1.5	2.2	5.8	8.6	14.4
Presenteeism (N = 324)	3.0	2.8	4.9	7.3	12.2
Overall work impairment (N = 290)	4.9	5.8	5.2	7.7	12.9
Activity impairment (N = 614)	8.7	8.8	5.0	7.5	12.5

\*P-value factor "change in anchor scores" <0.001;  $\Delta$  variation



preferential penetration into diseased versus normal tissue.<sup>1</sup> In this study we monitored metabolism of PEG in rats following subcutaneous administration of certolizumab pegol.

**Methods:** Subcutaneous injections of certolizumab pegol 400 mg/kg were given to nine female Lewis rats. The rats were housed in groups of three in metabolism cages for four 1-week periods (total study duration: 84 days). Daily urine and feces collections were weighed, and stored at  $-70^{\circ}\text{C}$  until analysis. PEG levels were quantified using proton nuclear magnetic resonance ( $^1\text{H}$  NMR) in urine samples purified by ultrafiltration.

**Results:** The mean recovery of PEG from urine and feces combined was 91% of the dose. PEG was detected in all urine samples; concentrations reached a maximum ( $198\text{ }\mu\text{g/mL}$ ) on Day 4, and then declined in a first-order manner to  $14\text{ }\mu\text{g/mL}$  in Week 12. The mean daily excretion in urine (as a proportion of the dose) was maximal (1.9%) on Day 6, declining in a first-order manner to 0.21% per day in Week 12. After 84 days, the mean cumulative amount of dose excreted in urine was 65%. Using a first-order increase/decrease model, the total urinary excretion was 73% and the half-life for the decrease in daily urinary excretion was 23 days. The molecular weight of the PEG excreted in urine was estimated by SDS PAGE to be 40 kDa. Up to Day 42, PEG equivalent to 18% of the dose was detected in feces (much of the fecal PEG is thought to be a result of urine contamination).

**Conclusion:** The innovative method of  $^1\text{H}$  NMR spectroscopy shows that, in the rat, the 40 kDa PEG moiety of certolizumab pegol is cleaved from the Fab' and excreted unchanged in a first-order process, predominantly in the urine. The half-life for excretion of a single dose determines the time taken to reach steady-state excretion on multiple dosing. The rate of excretion during multiple dosing matched the rate of dosing at steady-state as cumulative excretion was near-quantitative.

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## 965

### The Apparent Increase in Apoptosis Reported for Adalimumab, Etanercept, and Infliximab Is Actually a Reduction in Cell Proliferation

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**Purpose:** Induction of apoptosis in lymphocytes and monocytes by signaling through membrane tumor necrosis factor (TNF) is a proposed mechanism of action for anti-TNFs in Crohn's disease (CD). However, certolizumab pegol, an Fc-free PEGylated Fab' anti-TNF, is efficacious in CD but does not mediate an apparent increase in apoptosis in vitro. Although etanercept was initially reported not to cause apoptosis (and this was cited as the reason for its lack of efficacy in CD) three groups have now shown that etanercept does mediate apoptosis in a similar manner to infliximab and adalimumab. The precise mechanism of the apoptotic effect of some anti-TNFs and its importance to efficacy are unclear. This study investigated the apparent pro-apoptotic effects of adalimumab, etanercept, and infliximab in activated monocytes and lymphocytes.

**Methods:** Positive selection with MACS beads was used to separate monocytes from human peripheral blood mononuclear cells. The negatively selected population was used as the lymphocyte preparation. Monocytes were activated with GM-CSF and interleukin-4 for 3 days; lymphocytes were activated with CD3/CD28 for 2 days. Anti-TNFs or appropriate controls were then added (final concentration:  $10\text{ }\mu\text{g/mL}$ ) for a further 24 hours. The Vi-aCount assay system (Guava Technologies) was used to ascertain absolute cell counts and cell viability.

**Results:** The absolute number of apoptotic cells did not increase above the levels seen in the respective control samples after treatment of monocytes or lymphocytes with any of the anti-TNFs. However, adalimumab, etanercept, and infliximab reduced the number of viable monocytes (36.3%, 35.6%, and

38.3%, respectively) and lymphocytes (31.7%, 32.7%, and 32.5%, respectively) relative to controls. In contrast, certolizumab pegol did not cause a significant reduction in the number of viable cells compared with control treatment.

**Conclusion:** The anti-TNFs adalimumab, etanercept, and infliximab do not appear to increase apoptosis in isolated monocytes and lymphocytes; instead, they reduce the proliferation of these cells. However, since certolizumab pegol treatment does not reduce cell proliferation, anti-proliferative activity against monocytes and lymphocytes does not seem to be required for efficacy in CD. The mechanism of this effect is unclear and requires further investigation.

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## 966

### MR Enterography in Crohn's Disease: A Preliminary Experience

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**Purpose:** Patients with Crohn's disease often require multiple radiologic examinations throughout their lives beginning at a young age. MRI of the abdomen and pelvis can provide all of the necessary imaging information required for clinical management of Crohn's disease without the ionizing radiation associated with CT or SBFT as well as with a safer intravenous contrast medium (gadolinium vs. iodinated contrast). Here we report our initial experience with MR enterography in 11 patients with established or suspected Crohn's disease.

**Methods:** MR enterography was ordered at the discretion of the referring gastroenterologist. All examinations were performed on a 1.5 Tesla MRI scanner using a surface coil. Axial and coronal images were obtained using the following pulse sequences: steady-state free precession (an adapted cardiac imaging sequence), single-shot fast-spin echo (typically used for MRCP), as well as 3D fat-saturated gradient echo. 900 cc Volumes<sup>TM</sup> plus 450 cc of water were used for oral contrast to optimally distend the small bowel. Intravenous gadolinium was administered to all patients to delineate increased mucosal enhancement indicative of inflammation, as well as fistulae, phlegmons and abscesses. Total exam time was twenty minutes or less. The clinician then assessed the utility of the information provided by the MRI in managing the patient on a 3 point scale: 0 useless, 1 somewhat useful, 2 very useful. The first 11 patients referred for MR enterography are included.

**Results:** All the clinicians rated the MR enterography as very useful (2) in managing their patient(s). Findings included mucosal and mesenteric inflammation, small bowel strictures and fistulae. No abscesses were present. One MR exam was normal in a patient whom the clinician felt had been previously misdiagnosed. In this case, the normal study helped refute the diagnosis.

**Conclusion:** MR enterography was very useful in evaluating known or suspected Crohn's disease while eliminating patient exposure to ionizing radiation in this preliminary study. The examinations were well tolerated and provided diagnostic information directly relevant to patient management. Future, larger studies are needed to confirm our experience and also to determine whether MR can assess response to treatment in an accurate and timely fashion. This information, obtained without additional risk to the patient, could ensure that patients receive the optimal treatment for the appropriate duration.

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### Prevalence of Epstein-Barr Virus in Patients with Inflammatory Bowel Disease

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**Purpose:** Inflammatory bowel disease (IBD) (Crohn's Disease and Ulcerative Colitis) is characterized by chronic inflammation of the gastrointestinal tract. IBD is often treated with steroids, mesalamines, immunomodulators and biologics. With the increasing use of immunomodulators and biologics, concerns have been raised regarding the risk of development of lymphoma in IBD patients. The incidence of lymphomas in IBD is controversial. Studies from tertiary care centers seem to associate lymphomas with IBD. Epstein-Barr Virus (EBV), a herpes virus, has been associated with lymphomas in post-transplant and immunosuppressed patients. One major barrier to understanding etiology of this increased risk is delineating between disease activity, treatment and the possible role of oncogenic viruses. Our aim is to determine the prevalence of EBV in patients who are currently being followed in our IBD clinic compared to a selected group of controls.

**Methods:** 79 patients with IBD and 25 control subjects were studied. DNA was extracted from peripheral blood mononuclear cells (PBMC) of patients with IBD and from healthy IBD negative controls. Cell numbers were calculated using a CCR5 standard curve. EBV loads per million PBMC were determined using a real-time PCR assay.

**Results:** A higher incidence of EBV DNA was observed in the IBD positive group compared to the IBD negative group. EBV was detected in 49% of IBD patients and in 32% of controls. Results indicate higher average levels of EBV DNA in IBD positive patients ( $1.29 \times 10^8$  compared to  $1.76 \times 10^3$  copies/million PBMC).

**Conclusion:** The prevalence of EBV is higher in patients with IBD than that of controls. EBV viral load averaged 5 logs greater than that of controls. Contributing factors to these findings may include immunosuppressive medications, biologics and the severity of disease activity. Due to our smaller control sample size, the difference in EBV detection was not statistically significant ( $P = 0.13$ ). The significance of higher prevalence of EBV and higher EBV viral load will need to be determined in a prospective matter.

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#### NOD2/CARD15 Gene Exons Sequencing in Iranian Patients with Crohn's Disease

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**Purpose:** In this study all the exons of NOD2/CARD15 gene were sequenced in Iranian Crohn's patients to find any probable defect in this gene.

**Methods:** Sixty non-related Crohn's patients were enrolled from a tertiary center in a one year period (2006–2007). All 12 exons of NOD2/CARD15 gene were amplified by PCR (Polymerase Chain Reaction) and evaluated by direct sequencing.

**Results:** Of 9 sequence variations identified among 12 exons of NOD2/CARD15 gene, 4 had an allele frequency  $>10\%$ . Four new mutations (1 in exon 2 and 3 in exon 4) were observed, which account for less than 5% of NOD2/CARD15 mutations. The three main variants (R702W, G908R, and 1007fs) represented 32%, 5%, and 6%, respectively, in Iranian CD patients. Considering the whole sequence, mutations were mostly present in exon 4 of this gene.

**Conclusion:** Different mutations observed in NOD2/CARD15 gene demonstrated its importance in Iranian CD patients as western populations; though the affected parts would be different compared to other ethnicities.

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#### Non-Adherence to Surveillance Colonoscopy in Patients with Inflammatory Bowel Disease: Assessing the Risk

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**Purpose:** Patients with longstanding, extensive UC or Crohn's colitis have an increased risk of colon cancer and require colonoscopic surveillance every 2 yrs. The purpose of this study is to determine the non-adherence rate to surveillance colonoscopies in our patient population and to determine the risk factors that are associated with non-adherence.

**Methods:** 259 patients with UC or Crohn's colitis for at least 7 yrs and at least 1/3 of the colon involved participated in this cross-sectional questionnaire study. A chart review was also performed for each patient. Part of the questionnaire included a self-efficacy scale as it related to the ability to adhere to surveillance colonoscopy.

**Results:** Median age was 48 and median disease duration 20 yrs. 44% of patients had UC, and 51% were female. 49% of patients had waited more than 2.5 yrs in between exams and 40% of patients had waited longer than 3 yrs in between exams. Self-reported adherence was higher than chart-documented adherence for all times in between exams. Patients who self-reported less than 6 months in between exams had a mean chart-documented adherence of 2.16 yrs in between exams. For self-reported frequencies of 1, 2, and 3 yrs or more in between exams, the chart documented mean time intervals between exams were every 2.08, 3.16, and 4.32 yrs respectively.

We validated our large self-efficacy (SE) scale and divided it into 4 subscales, all significant and valid: Social SE (ability to schedule, tell people, avoid embarrassment), Calm SE (ability to avoid anxiety associated with colonoscopies), Prepare SE (ability to take and to tolerate the preparation), and Doc Comm SE (ability to get doctor's attention and to ask questions). Both Calm and Social SE were associated positively with adherence, and Prepare and Doc Comm SE correlated positively with lower average time between screenings. Patients reporting that they have trouble with the preparation and scheduling, that they felt good and did not think the test was needed, and that they have had inadequate insurance coverage were less likely to adhere. By logistic regression, being Jewish, having high Social SE, and using alternative health care methods were positively related to adherence.

**Conclusion:** At least 40–49% of patients do not adhere to surveillance colonoscopies. Many factors relate to adherence including demographic and clinical factors, doctor message, and self-efficacy.

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#### Younger Age at Diagnosis Predicts Disease Severity in Ulcerative Colitis

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**Purpose:** Canada has one of the highest incidences of ulcerative colitis (UC) in the world, with 3500 new cases each year and a prevalence of over 60,000†. Previous studies have examined the natural history of UC, however, this is the first to examine it in Southwestern Ontario (SWO). London is uniquely situated with a catchment area of nearly all of SWO, and the London Health Sciences Centre – South Street Hospital (LHSC-SSH) Inflammatory Bowel Disease (IBD) clinic is set up to longitudinally follow patients who are diagnosed and treated there. The goal of the current study is to understand the demographic characteristics of this population in order to predict disease severity. †Am J Gastro 2006;101:1559–68.

**Methods:** Records from 1996 to 2001 were examined to create a database of UC patients seen in the LHSC-SSH IBD clinic. To be included, patients' charts were required to have information of their disease presentation and a minimum of five years of follow-up. Charts were reviewed using standardized data collection forms. Disease severity was generated during the chart review process, and non-endoscopic Mayo Severity Index‡ criteria were collected into a composite. ‡NEJM 1987;317:1625–9.

**Results:** 102 consecutive patients' data were entered into the database. Demographic analyses revealed that 51% of the patients were male, the mean age at diagnosis was 39 years, 13.7% had a first degree relative with IBD, 61.8% were nonsmokers and 24.5% were ex-smokers. In 22.5% of patients the disease was limited to proctitis, 21.6% had proctosigmoiditis, 22.5% had left-sided colitis, and 32.4% had pancolitis. Standard multiple regression

analysis which regressed a composite of physician global assessment of disease severity, average number of bowel movements, and average amount of blood in bowel movements on year of diagnosis and age at time of diagnosis was significant,  $R^2 = .306$ ,  $F(7, 74) = 4.66$ ,  $P < .01$ . Delay from symptoms to diagnosis of UC, gender, family history of IBD, smoking status and disease severity at the time of diagnosis did not significantly predict the composite measure.

**Conclusion:** A composite of UC disease severity, blood in bowel movements, and number of bowel movements is associated with younger age at diagnosis as well as year of diagnosis in a longitudinal cohort of UC patients in SWO. This suggests a potential mechanism for predicting disease severity at diagnosis and may be a step towards the identification of prognostic indicators of UC.

## 971

**Efficacy and Safety of Certolizumab Pegol Do Not Appear To Be Affected by Neutralizing Antibodies in Patients with Crohn's Disease**  
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**Purpose:** Anti-TNF agents are effective in the treatment of Crohn's disease (CD). However, development of neutralizing antibodies can potentially reduce the clinical response rate.<sup>1</sup> Certolizumab pegol, a PEGylated Fc-free Fab' with high potency for human TNF $\alpha$ , was evaluated in two recent pivotal Phase III trials in CD (PRECISE 1 and 2) in which the effect of neutralizing antibodies on efficacy and safety was analyzed.

**Methods:** Subcutaneous certolizumab pegol 400 mg was administered at Weeks 0, 2, 4, then every 4 weeks up to Week 24. Plasma samples were considered neutralizing if they reversed the ability of certolizumab pegol to block interleukin-6 production in response to TNF $\alpha$  in HeLa cells. Patients with  $\geq 1$  neutralizing sample were classed as antibody positive (Ab+). Clinical response was defined as a decrease in CD Activity Index (CDAI) score of  $\geq 100$  points (at Weeks 6 and 26 PRECISE 1 and Week 26 in PRECISE 2). Influence of antibody status on the incidence of adverse events (AEs) was also examined.

**Results:** Clinical response rate by neutralizing antibody status was determined for patients who received continuous treatment with certolizumab pegol (Table). There was no reduction in the proportion of responders in the Ab+ cohort relative to the antibody negative (Ab-) cohort in either trial. Most AEs occurred with a similar incidence regardless of neutralizing antibody status. AEs that occurred more frequently in patients after development of antibodies were viral gastroenteritis (3% [Ab+] vs 1% [Ab-]) and anemia (5% vs 3%). AEs occurring more frequently in Ab- patients were nausea (9% [Ab-] vs 2% [Ab+]), pyrexia (8% vs 4%), and headache (17% vs 5%). No hypersensitivity signals (eg, injection-site reactions, injection-site pain, influenza-like illness or rash) were associated with the presence of antibodies.

	PRECISE 1 (Weeks 6 and 26)		PRECISE 2 (Week 26)	
	Ab+	Ab-	Ab+	Ab-
Clinical response, n/N (%)	6/21 (28.6)	69/304 (22.7)	10/12 (83.3)	123/201 (61.2)

**Conclusion:** The development of neutralizing antibodies to certolizumab pegol does not appear to have a marked effect on clinical response rates in patients with CD. The frequency of AEs was similar in Ab- and Ab+ patients. Patients in this trial showed no indication of hypersensitivity reactions.

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## 972

**PROTECT-1: A Prospective Randomized Trial of CCX282-B (Traficet-EN), a Novel Oral Therapy Targeting Chemokine Receptor 9 in Crohn's Disease**

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**Purpose:** CCX282-B represents a new class of highly specific chemokine receptor antagonists. It targets chemokine receptor 9 (CCR9), a key homing signal for intestine-specific T cells. In a 28-day phase 2 study, CCX282-B induced clinical responses (CDAI $\Delta$ 70) in 58% of Crohn's disease (CD) patients with a baseline CDAI  $>250$  and elevated CRP, vs. 31% on placebo. CRP decreased 11 mg/L in the CCX282-B group relative to placebo. These results prompted PROTECT-1, a large, randomized, placebo-controlled trial in CD.

**Methods:** This study involves  $>100$  sites in 16 countries. The primary efficacy endpoint is CDAI decrease over 12 weeks. Maintenance of response is assessed over 36 weeks. Adults with moderate to severe CD (CDAI 250–450), are randomized 3:2:2 to receive placebo, CCX282-B 250 mg/day, 500 mg/day, or 250 mg twice daily (bid) for 12 weeks followed by a 4-week Active Treatment period (250 mg CCX282-B bid). CDAI $\Delta$ 70 responders are then re-randomized 2:3 to receive either placebo or 250 mg CCX282-B bid for 36 weeks (Maintenance period).

**Results:** As of May 2007, 163 subjects have been enrolled into the Induction Period. 56 subjects have enrolled into the Active Treatment period. 39 subjects have completed the Active Treatment period, of which 29 (74%) have achieved a CDAI $\Delta$ 70 response, 27 (69%) a CDAI $\Delta$ 100 response, and 16 subjects (41%) were in remission (CDAI  $<150$ ). No serious unexpected adverse events related to CCX282-B have been observed, and overall more than 250 subjects have received CCX282-B in clinical trials, with no adverse safety concerns.

**Conclusion:** CCX282-B, a highly specific, oral CCR9 antagonist, and the first chemokine-based inhibitor of leukocyte trafficking tested in IBD, shows promise in CD.

## 973

**Prevalence and Predictors of Sexual Dysfunction in Patients with Inflammatory Bowel Disease**

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**Purpose:** Little is known about sexual dysfunction in pts with inflammatory bowel disease (IBD). Our aim was to assess the prevalence and factors associated with sexual dysfunction among pts with IBD.

**Methods:** A clinical sample from a tertiary referral center was interviewed during their routine clinic visit. The Sexual History Form and questions

that assess sexual well-being from the National Health and Social Life Survey were used to determine the prevalence and severity and a global sexual functioning score (GSFS) was calculated (0.11 = perfect functioning; 1 = significant dysfunction). IBD severity was assessed using the Short Form IBDQ (S.IBDQ). The cohort results were compared to historic controls from both surveys. Non-parametric tests were used to assess associations and multivariate analysis was performed to control for potential confounders.

**Results:** 62 IBD pts; 46 (75%) pts with CD and 16 (25%) with UC with a mean age of 44 (range 18 to 74 years) with a mean S.IBDQ score of 50 (range of 22 to 70 at the time of the survey) were surveyed. Sexual dysfunction was more prevalent in patients with IBD than the general public (68% vs 31% with any degree of dysfunction;  $P = 0.002$  and 38% vs. 12% with significant dysfunction;  $P < 0.0001$ ). Mean GSFS was significantly worse among IBD pts compared to values reported in general public (0.51 vs 0.22;  $P = 0.008$ ). Multivariate analysis showed that this dysfunction did not correlate and was independent of underlying IBD activity as measured by the S.IBDQ, steroid use in the past 6 months, disease duration and history of previous surgery. Furthermore, only one pt received counseling regarding this problem (self-referred).

**Conclusion:** Sexual dysfunction is an important concern in patients with IBD, and must be addressed while treating the patient for their disease. This dysfunction appears to be independent of disease activity and other disease related factors. Further studies to determine potential causes including psychiatric and / or endocrine evaluation should be considered.

## 974

#### The Direct and Indirect Cost Burden of Illness of Ulcerative Colitis

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**Purpose:** To estimate the direct medical costs and indirect costs (productivity related) for commercially-insured patients with Ulcerative Colitis.

**Methods:** Data were obtained from the 1999 to 2005 MarketScan Commercial Claims and Encounters (CCAE), Medicare Supplemental, and Health and Productivity Management databases. Patients with a diagnosis of Ulcerative Colitis and at least a 1-year disease-free pre-period were found resulting in 8,970 nonelderly patients with Ulcerative Colitis and 2,958 elderly patients with Ulcerative Colitis. 12-month direct medical care expenditures (medical and prescription drug) for patients with Ulcerative Colitis were compared to expenditures among an equal number of propensity-score matched comparison group members. Propensity scores were estimated via demographic characteristics and comorbidities. Indirect costs, as measured by absenteeism and short-term disability costs, were compared for a sub-sample of employees in each group. Regression analysis controlled for demographic and case mix factors. A range of cost burden estimates were produced by varying the estimation and matching techniques.

**Results:** Average 12-month direct medical care expenditures were \$4,982 for nonelderly and \$8,572 for elderly comparison group members. Average estimated direct medical expenditures for patients with Ulcerative Colitis exceeded comparison group members by as much as \$11,331 for nonelderly patients and \$6,609 for elderly patients (all  $P < .01$ ).

Average absenteeism costs were \$6,021 for employees with Ulcerative Colitis, although this was not significantly different from the comparison group. Average short term disability expenditures were \$1,386, which was almost three times the amount for the comparison group ( $P < .05$ ).

**Conclusion:** Ulcerative Colitis is a costly disorder and merits consideration as interventions are developed to manage the burden of disease and improve productivity.

## 975

#### Clinical Predictors of Elevated C-Reactive Protein (CRP) among Patients with Active Inflammatory Bowel Disease

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**Purpose:** CRP is a useful inflammatory marker frequently used in the management of inflammatory bowel disease (IBD) pts. However, certain groups of pts have either normal or slightly elevated CRP despite significantly active disease.

Our aim was to identify determinants of CRP levels in IBD pts.

**Methods:** Pts with confirmed IBD and at least 2 of the following indicators of active disease (radiologic, endoscopic, pathologic or clinical) were included in the study. CRP level at the time of disease activity was measured. Demographics and disease characteristics including location, modifiers and phenotype were assessed. Non-parametric tests were used to assess associations and multivariate analysis was performed to find independent predictors.

**Results:** 92 pts (64 with CD and 28 with UC), mean age 36 yrs (14–68) and mean age at diagnosis 27 yrs (9–62) were included in the study. Mean CRP level in the cohort was 3.9 mg/dl (0.3–21.4) and 14 pts had levels >10. CD and UC pts had comparable mean CRP level (3.2 vs 5.5;  $P = \text{ns}$ ) Univariate analysis showed that among CD pts, colonic involvement was associated with higher CRP level compared to ileal disease only (1.7 vs 3.8;  $P = 0.01$ ) and active perianal disease compared to no perianal involvement (1.4 vs 4.9;  $P = 0.005$ ). Stricturing phenotype was associated with lower mean CRP (1.1) compared to fistulizing (5.3) and inflammatory (3.7) phenotypes ( $P = 0.02$ ). Among UC pts, pancolitis was associated with higher CRP level compared to pts with Lt sided or proctitis (5.1 vs 2.7;  $P = 0.02$ ). In the entire group, older age at diagnosis was associated with higher CRP ( $P = 0.02$ ). Neither smoking nor family history were associated with CRP level. All associations remained significant in the multivariate analysis.

**Conclusion:** Colonic and perianal involvement in CD pts is associated with high CRP levels while stricturing phenotype and ileal disease are associated with lower levels. Among UC pts, pancolitis is associated with higher CRP levels. In IBD pts, in general, older age at diagnosis is associated with higher CRP levels. These characteristics may help to identify a group of patients in whom CRP can be used reliably to assess activity and follow response to treatment.

## 976

#### Predictors of Short and Long Term Response to Azathioprine in Crohn's Disease

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**Purpose:** Azathioprine (AZA) is widely used in the treatment of pts with Crohn's disease (CD). Despite appropriate dosing and the use of metabolite levels monitoring to guide therapy many pts fail to respond to AZA or have short remission periods.

**Aim:** To identify factors associated with short and long term response to AZA.

**Methods:** Using our IBD database we identified CD pts treated with AZA for at least 3 mos. Short-term response was defined as adequate subjective and objective control of disease (determined by IBDQ scores and the global assessment of pt and physician) and the ability to wean off steroids in pts requiring steroids. Long-term response was defined as quiescent disease for  $\geq 1$  year. Pts requiring other therapeutic modalities (including surgery) during the time frames outlined were also considered to have had no or lost response. AZA dose used in our institution is 2–2.5 mg / kg/ day or its equivalent of 6-MP. Pts with TPMT phenotype other than wild were excluded. A case-control design was implemented. Non-parametric tests and logistic regression models were used to assess the associations, estimate the odd ratio

(OR) and 95% confidence intervals (CI) of these associations and control for potential interactions (AZA dose and concomitant medications).

**Results:** 148 CD pts treated with AZA were identified for assessing short-term response to AZA and 97 pts for long-term response. Among pts assessed for short term response, 106 (72%) had short term response while 42 (28%) did not and had to be treated with another immunomodulator. Among pts assessed for long term response, 62 (64%) pts had sustained response while the rest (35; 36%) did not. Smoking was associated with decreased short and long-term response (OR 2.4 & 1.8; 95% CI:1.6–5.9 & 1.4–5.2 respectively). Infliximab maintenance therapy was associated with long-term response (OR 2.0; CI:1.6–7.8) while concomitant use of 5-ASA compounds was associated with short term response: OR: 1.5; CI:1.1–2.9. Long term responders were significantly older at diagnosis than non responders (median age was 32 vs. 25 yrs;  $P = 0.02$ ).

**Conclusion:** Smoking is associated with decreased short and long term response to azathioprine in Crohn's disease patients while Infliximab maintenance therapy and older age at diagnosis are associated with a longer response.

977

### Mesalamine Protects Against Colorectal Cancer in Inflammatory Bowel Disease

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**Purpose:** Individuals with ulcerative colitis (UC) and Crohn's disease (CD) are at increased risk of developing colorectal cancer (CRC) compared to the general population. CRC risk in inflammatory bowel disease (IBD) is associated with dysplasia, extent of disease, type of therapy, duration of disease, and degree of inflammation. This study evaluates the influence of multiple factors on CRC risk in IBD.

**Methods:** We identified all IBD patients who developed CRC at our institution from 1970 to 2005. Cases were matched to controls by type of IBD, age at diagnosis, sex, race, extent of disease and disease duration. We compared BMI, family history of IBD, family history of CRC, smoking, and use of mesalamine, mercaptopurine, folic acid, steroids, and nonsteroidal anti-inflammatory drugs (NSAIDs). Total cumulative dose and average daily dose were calculated for each prescription drug class. Covariates were compared using Chi-square and Student's t-tests. Odds Ratios (OR) and 95% confidence intervals (CI) were estimated using conditional logistic regression models to examine the relationship between drugs and risk of colorectal cancer.

**Results:** A total of 30 CRC patients (25 UC [16 male, 9 female; 37.8 mean age] and 5 CD [3 male, 2 female, 42.2 mean age]) were identified. After reviewing 1484 patients (605 UC and 879 CD), 16 patients (13 UC and 3 CD) were matched to 23 controls (19 UC and 4 CD). The CRC cases and controls were similar in BMI (mean, 27.5 vs. 25.0), family history of IBD (18.8 vs. 8.8% positive history), family history of CRC (18.8 vs. 8.8% positive history), and smoking use (66.7 vs. 52.2% nonsmoker). There was no difference in use of mercaptopurine (6.3 vs. 13.0%), NSAIDs (6.7 vs. 21.7%) and steroids (80.0 vs. 82.6%). More controls used folate compared to the CRC cases (56.5 vs. 20.0%,  $P = 0.025$ ). Mesalamine use in UC showed a decrease in CRC when comparing the cases and controls (76.9 vs. 100%,  $P = 0.028$ ). Conditional logistic regression showed that a mesalamine total dose of  $\geq 5068$  grams was associated with an 89% reduction in CRC risk

(OR 0.11; CI 0.01–0.91). Folate use at cumulative dose of  $\geq 2823$  mg did not show a significant reduction in CRC risk (OR 0.47, CI 0.09–2.50).

**Conclusion:** Our data suggest that mesalamine use among UC patients leads to a significant risk reduction in CRC. In our study we found that patients that did not develop CRC used folate more often than those with CRC but this was not associated with a reduction in risk of CRC.

978

### Distal Location of Dysplasia and Colorectal Cancer in Longstanding Ulcerative Colitis (UC)

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**Purpose:** Current guidelines recommend that surveillance for dysplasia be performed by taking 4-quadrant biopsies every 10 cm throughout the colon in patients with longstanding UC. Such a strategy, however, may be ineffective if neoplastic lesions arise only in particular segments of the colorectum.

**Aim:** To determine where in the colorectum advanced neoplastic lesions are detected in the practice of surveillance colonoscopy.

**Methods:** The Mount Sinai UC-Dysplasia Surveillance Database in an IRB-approved project that contains clinical, endoscopic, and pathologic information on more than 700 patients at our institution who have undergone 2 or more dysplasia surveillance exams between 1994 and 2006. To determine the location of biopsies containing advanced neoplasia (AN; colorectal cancer (CRC) or high-grade dysplasia (HGD)) the database was queried. Pathology reports were then reviewed and the locations of all the AN lesions were tabulated. In instances where distances were used to describe biopsy location, jars labeled 0–20 cm were considered rectal in origin; 21–40 cm sigmoid; 41–60 descending colon; and  $\geq 61$  cm transverse colon. The frequency with which any segment was positive was then compared to other segments. Comparisons were made using Fisher's exact testing with  $P < .05$  significant.

**Results:** We identified 54 patients who progressed to AN. They underwent a total of 283 exams. The mean age of the patients at first surveillance was 49.6 years; the mean duration of disease was 18.3 years; 80% of the patients had UC proximal to the splenic flexure. The percent of biopsies that were positive for AN by location is listed in the Table. Biopsies positive for AN were much more common in the rectum and sigmoid colon than in more proximal segments ( $P < .0001$  for all two-way comparisons).

**Conclusion:** The majority of HGD and cancer detected in a surveillance program was detected in the rectum and sigmoid. Endoscopists should consider taking a greater percentage of their biopsies from these segments.

979

### A Pilot Study of the Efficacy and Tolerability of AST-120 in the Treatment of Active Pouchitis

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**Purpose:** Bacterial toxins and increased production of deconjugated bile acids are speculated to play a role in the pathogenesis of pouchitis. While the majority of patients with pouchitis respond to antibiotics, relapse is common and non-absorbable and non-antibiotic-based agents are desirable to reduce bacterial resistance and systemic adverse effects associated with

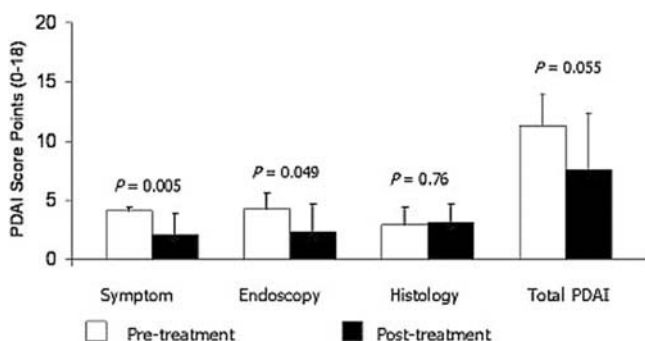
Location	Ascending Colon/ Cecum	Transverse Colon	Descending Colon	Sigmoid	Rectum
Number of specimen jars from site	955	1361	550	677	736
% Positive for HGD/CRC	1.3	1.2	1.5	5.6	9.4

long-term antibiotic use. AST-120 is comprised of highly adsorptive, porous, carbon microspheres with the ability to adsorb small molecular weight toxins, inflammatory mediators, and harmful bile acids. The aim of this pilot study was to evaluate efficacy and tolerability of AST in the treatment of active pouchitis.

**Methods:** Inclusion criteria: 1) active pouchitis patients with underlying ulcerative colitis (UC) with Pouchitis Disease Activity Index (PDAI) scores  $\geq 7$ ; and 2) discontinuation of antibiotic therapy for at least 2 weeks. Exclusion criteria included Crohn's disease of the pouch, and isolated cuffitis. In this open-label study, all eligible patients received AST-120 in 2 g sachets PO tid for 4 weeks. The efficacy endpoints were remission (PDAI score  $< 7$ ) and clinical response (reduction of PDAI score of  $\geq 3$ ). Cleveland Global Quality of Life (QOL) and Short Inflammatory Bowel Disease Questionnaire were also assessed before and after the trial.

**Results:** Ten patients were enrolled the trial: 9 completed the trial (mean age =  $50 \pm 10$  yrs, SD; mean duration of UC =  $16 \pm 9$  yrs; mean duration of ileal pouch =  $7 \pm 5$  yrs) and one dropped out of the trial due to a viral upper respiratory infection 2 days after entry. Of the 9 patients, 4 (44%) had clinical remission and 5 (56%) achieved clinical response and (AST-120 effect on components of the PDAI illustrated below). There was numerical, but not statistically significant improvement in QOL scores. The agent was well tolerated; one patient had transient mild elevation of alkaline phosphatase.

**Conclusion:** AST-120 appears to be effective and well tolerated in treating patients with active pouchitis. A randomized, placebo-controlled trial is warranted to assess long-term efficacy and safety of AST-120 in this indication.[figure1]



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#### A Pilot Study of the Effects of Dietary Soy Supplementation on Crohn's Disease

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**Purpose:** Crohn's disease is a chronic inflammatory disorder of the gastrointestinal tract and dietary therapy has been studied to modulate the inflammatory cascade and treat Crohn's disease. Soy contains several substances with anti-inflammatory activity such as isoflavones. The aim of this study is to investigate the efficacy and tolerability of dietary soy supplementation in patients with Crohn's disease.

**Methods:** Patients with Crohn's disease, active or inactive, who were seen at the Wake Forest University Digestive Health Center were asked to participate in a prospective open-label pilot study of soy supplementation. After a full history and physical with labs, each subject had a C-reactive protein (CRP) recorded, a Crohn's Disease Activity Index (CDAI) calculated, and an Inflammatory Bowel Disease Questionnaire (IBDQ) performed. Subjects were asked to ingest a proprietary, flavored soy shake (Physicians Laboratories, Kernersville, NC) twice a day for 12 weeks. Subjects were followed by telephone every 3 weeks and with a clinic visit every 6 weeks. CRP, CDAI, and IBDQ were followed at 6 and 12 weeks. Any subject with worsening Crohn's disease requiring new drug therapy was withdrawn from the trial.

**Results:** Ten patients were enrolled, and then enrollment was halted. Five patients were unable to tolerate two shakes a day and discontinued the study by week 6 and one additional patient discontinued the study after week 6. Of the 4 patients who completed the study, 3 were in remission at baseline and stayed in remission, while one patient with mildly active disease continued to have mildly active disease at week 12. No changes in CRP, CDAI, or IBDQ were seen.

**Conclusion:** While dietary therapy is an appealing strategy in the management of Crohn's disease, the preparation and dose used in this study was not well tolerated and the study was unable to show benefit.

981

#### Elevated CRP (C-Reactive Protein) Levels Can Predict Ileal Involvement in Patients with Inflammatory Bowel Disease

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**Purpose:** The advent of high-sensitivity CRP (hs-CRP) has enabled us to detect disease activity in patient with IBD. We sought to examine the relationship between hs-CRP (CRP) and location of disease in IBD based upon endoscopic, histologic, and radiographic activity.

**Methods:** All IBD patients at our institution between July 2000 and June 2006 who had a CRP, and colonoscopy with biopsy and/or small bowel follow through (SBFT) performed with 90 days were identified, retrospectively. The diagnosis of Crohn's disease (CD) or Ulcerative Colitis (UC) must have been made or confirmed at our institution. Those patients who underwent proctocolectomy with IPAA were excluded from the study. The patients with CD and UC were separately identified and the odds ratio (OR) for an elevated CRP was determined based upon location of disease.

**Results:** A total of 218 patients with a confirmed diagnosis of IBD were identified of which 93 patients fulfilled the inclusion criteria. Of the 53 patients with CD, the mean CRP was 2.80 mg/dL, regardless of disease location. Using a cutoff CRP level of 2.0 mg/dL, the odds ratio (OR) for terminal ileum involvement was 3.38, suggesting that those CD patients with a CRP greater than 2.0 mg/dL are more prone to have ileal involvement. Of the 40 patients with UC, the mean CRP was 3.18 mg/dL, independent of location of disease. Again, using a cutoff CRP level of 2.0 mg/dL, the odds ratio (OR) for ileal involvement was 3.29. The data suggests that a CRP level greater than 2.0 mg/dL predicts backwash ileitis in those patients with UC. Interestingly, those patients who had CRP levels greater than 7.0 mg/dL were found to have Cytomegalovirus infection in the colon, Clostridium difficile infection, or another underlying systemic infectious process.

#### Elevated CRP and Risk of Ileitis

	Crohn's Disease		Ulcerative Colitis	
	Ileitis ± Colitis	No Ileitis ± Colitis	Ileitis ± Colitis	No Ileitis ± Colitis
CRP < 2 (mg/dL)	25 (66%)	13 (34%)	4 (15%)	23 (85%)
CRP > 2 (mg/dL)	13 (87%)	2 (13%)	4 (36%)	7 (7%)
Odds Ratio	3.38		3.29	

**Conclusion:** CRP elevation in Inflammatory Bowel Disease is associated with active disease determined endoscopically, histologically, or radiographically. In both CD and UC, a CRP > 2.0 mg/dL predicts findings of active ileal disease at ileocolonoscopy. Ileitis may play a crucial role in the inflammatory cascade of IBD.

982

### A Randomized Prospective Trial of Endoscopic Ultrasound (EUS) To Guide Combination Medical and Surgical Treatment for Crohn's Perianal Fistulas

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**Purpose:** To prospectively determine if rectal EUS can guide combination medical and surgical therapy and improve outcomes for patients (pts) with perianal fistulizing Crohn's disease.

**Methods:** 10 pts with perianal Crohn's disease were prospectively enrolled in a randomized prospective pilot study. Pts were randomized to either the EUS cohort or control group. All pts underwent a rectal EUS to delineate fistula anatomy followed by an exam under anesthesia by a colorectal surgeon with seton placement and/or incision and drainage as indicated. The surgeon was blinded to the initial EUS results of pts in the control group. Medical treatment was maximized with 6-MP or azathioprine, cipro or metronidazole, and infliximab [5 mg/kg at 0, 2, 6 weeks (wks) and q 8 wkly]. For pts in the control group, additional interventions (seton removal, repeat surgery) were at the discretion of the surgeon (without EUS guidance). Pts in the EUS cohort had EUS performed every 16 wks with additional surgical interventions based on EUS findings. The primary endpoint was complete cessation of drainage at wk 54. All pts had a repeat EUS performed at wk 54 to determine fistula status on EUS (secondary endpoint). The need for additional surgery was defined as a treatment failure.

**Results:** 10 pts enrolled in the study. One of the control pts by 3.5 mos into the study period required multiple repeat surgeries for recurrent fistulas/abscesses and is considered a treatment failure. 1/5 (20%) in control group and 4/5 (80%) in the EUS group have had complete cessation of drainage. From the control group, 3 pts failed due to repeat surgery (2 for persistent/recurrent fistula and 1 for abscess), and 1 had persistent drainage at wk 54. In the EUS cohort, 1 pt had recurrent abscess after his seton fell out prematurely.

In the EUS cohort, the median time to cessation of drainage was 99 days and the time to EUS evidence of fistula inactivity was 229 days.

**Conclusion:** In this pilot study, using EUS to guide combination medical and surgical therapy for perianal fistulizing Crohn's disease improves outcomes

983

### Inflammatory Bowel Disease in Afro-Caribbeans: Does It Differ from Other Ethnic Groups?

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**Purpose:** Recent studies in inflammatory bowel disease (IBD) have found phenotypic differences among ethnic groups. Limited data have been published about IBD patients of Afro-Caribbean (AC) origin. This study compares Afro-Caribbean IBD patients with three other ethnic groups.

**Methods:** Retrospective study of 73 AC IBD patients, first and second generation, followed in the GI clinic. Data were compiled based on sex, diagnosis, age at onset/diagnosis, family history of IBD, disease distribution and pattern, and extra-intestinal manifestations. Results were compared to those of the large North American Cohort Study of IBD patients, which included African Americans (AA), Whites and Hispanics. Data on Crohn's disease (CD) and ulcerative colitis (UC) distribution, pattern, and extent were ex-

tracted using the same criteria described by the large North American Cohort study.

**Results:** Differences were noted between AC patients and White, AA and Hispanic patients in regard to diagnosis, age at onset/diagnosis and family history of IBD (table).

AC have significantly less ileo-colonic CD compared with Hispanics and significantly more CD colitis compared with the other groups. No upper gastrointestinal involvement was seen in AC; this significantly differs from Whites and AA. No significant difference was found in CD pattern or UC disease extent among AC and the other groups.

IBD Phenotype in AC Compare with other Ethnic Groups from The Large North American Cohort Study

	White	AA	Hispanic	AC
Race distribution	809	116	168	73
Age at diagnosis, mean (SD) <sup>a</sup>	26.6 (12.8)	26.6 (13.3)	25.4 (13.2)	38.5 (14.4)
Female, No (%)	427 (51.5) <sup>b</sup>	80 (63)	77 (45.6) <sup>c</sup>	50 (68.5)
Family history of IBD (%) <sup>d</sup>	237 (29.3)	23 (19.8)	28 (16.7)	1 (1.5)
CD (%) <sup>e</sup>	510 (63)	81 (69.8)	106 (63.1)	26 (35.6)
UC (%) <sup>e</sup>	299 (37)	35 (30.2)	62 (36.9)	47 (64.4)

<sup>a</sup> Bonferroni-adjusted  $P < 0.001$  comparing AC with any of the other groups. <sup>b</sup>  $P = 0.013$  comparing AC with Whites. <sup>c</sup>  $P = 0.003$  comparing AC with Hispanics. <sup>d</sup>  $P < 0.0001$  comparing AC with Whites;  $P = 0.0003$  comparing AC with AA;  $P = 0.0013$  comparing AC with Hispanics. <sup>e</sup>  $P < 0.0001$  comparing AC with Whites and AC with AA;  $P = 0.0002$  comparing AC with Hispanics.

**Conclusion:** This is the largest series of AC IBD patients described in the literature. We found phenotypic differences among AC with IBD compared with other ethnic groups. The differences are likely related to genetic and environmental factors. A better understanding of these differences may influence patient management and disease prognosis.

984

### Infliximab Reduces Colectomy in Patients with Moderate-to-Severe Ulcerative Colitis: Analysis from ACT 1 and ACT 2

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**Purpose:** We assessed the incidence of colectomy through 54 wks, a follow-up to ACT 1 & ACT 2.

**Methods:** The prespecified primary analysis was time to colectomy in pts treated with infliximab (IFX) compared w/ placebo (PBO) (combined studies & IFX grps). Data were collected in ACT 1 & 2, ACT extension, & RESULTS-UC. Missing data were collected retrospectively. Rates of colectomy, UC-related hospitalizations, and UC-related surgeries and procedures were compared btw combined IFX and PBO. Stratified log-rank test was used for time to colectomy analysis, and Kaplan-Meier (K-M) product-limit estimated cumulative incidence of colectomy.

**Results:** 630 (86.5%) pts had complete colectomy follow-up; more IFX pts had complete colectomy follow-up (90.1%, 5 mg/kg; 86.8%, 10 mg/kg)

than PBO pts (82.8%). 81 pts (36, PBO; 27, 5 mg/kg; 18, 10 mg/kg IFX) had a colectomy thru 54 wks. The proportion of PBO pts who received commercial IFX prior to colectomy was higher than that for combined-IFX pts (15.7% vs 6.6%) in ACT 1, but similar in ACT 2 (6.5% vs 5.0%). Primary endpt: Cumulative incidence of colectomy (K-M) was significant favoring the combined-IFX grp,  $P = 0.012$ . The hazard ratio btw PBO and combined-IFX grps was 0.57 (95% CI: 0.37, 0.89), a 43% risk reduction in colectomy thru 54 wks. Major secondary endpts: A significantly greater proportion of PBO pts (14.8%) had colectomy than combined-IFX pts (9.3%,  $P = 0.028$ ) thru 54 weeks. The proportion of UC-related hospitalizations and surgeries were significantly higher in the PBO grp than those in the combined-IFX grp ( $P = 0.003$  vs  $P = 0.022$ ) through 54 wks after first infusion.

**Conclusion:** IFX significantly reduced the incidence of colectomy and decreased UC-related hospitalizations and UC-related surgeries/procedures compared with PBO in UC.

## 985

### Gastroenterologists' Practices and Attitudes Regarding Inflammatory Bowel Disease

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**Purpose:** To assess organizational and MD-based aspects of IBD practice variation within a multi-site integrated care delivery system and the extent to which physicians are interested in adopting a chronic care model and/or nurse assistance to manage IBD patients.

**Methods:** As part of an observational cohort study to understand variation in IBD care and outcomes, we conducted semi-structured, open-ended interviews with 17 gastroenterologists and 1 gastroenterology nurse at 6 clinics in 1 Northern California integrated care delivery system. All interviews were tape recorded and transcribed. We coded and analyzed transcripts using standard qualitative methods.

**Results:** Physicians reported a range of IBD practice among and between clinics. Data analysis showed most notable differences in 4 domains: 1) *primary care involvement*: the extent to which internists conduct initial work-ups and co-manage patients with mild disease; 2) *gastroenterologists' practices*: the extent to which gastroenterologists utilize practice guidelines and on-line sources; the degree to which colleagues confer with each other, surgeons, and acknowledged IBD experts; varying practices and attitudes regarding health education materials that are distributed and/or should be available for newly diagnosed patients; varying practices prescribing infliximab; and estimates ranging from < 5% to 50% for medical hospitalizations; 3) *patient factors*: use of alternative medicine is typically non-problematic and limited to urban areas; 4) *physician attitudes toward ancillary support*: the degree to which gastroenterologists feel there is potential for IBD specialty clinics or chronic care management and how this reflects physicians' beliefs that IBD is very much an "art of medicine" disease; and the potential value of using RNs for patient tracking.

**Conclusion:** 1. Standardized algorithms on how to care for IBD patients do not exist. 2. There is opportunity to improve or optimize IBD care by having initial work-ups and management of patients in remission in primary care and creating and maintaining opportunities for gastroenterologists to confer

with local colleagues, surgeons, and acknowledged local experts. 3. There is value in nurse coordination regarding medications and labs and/or some type of specialty IBD clinic for especially sick and/or newly diagnosed patients.

## 986

### Incidence of Post-Surgical Complications among Ulcerative Colitis (UC) Patients (Pts): A Population-Based Study

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**Purpose:** We sought to describe the incidence of and factors associated with post-colectomy complications among UC pts in Olmsted County, Minnesota.

**Methods:** We identified all pts who had undergone  $\geq 1$  surgery for UC in a cohort diagnosed with UC between 1970–2001. Colectomies were classified as: total proctocolectomy (TPC) with ileal pouch-anal anastomosis (IPAA), subtotal colectomy (SC) with ileostomy, TPC with ileostomy, and partial colectomy (PC). We examined post-colectomy complications by colectomy type. The association between colectomy type and time to first complication was assessed with proportional hazards regression analysis.

**Results:** A total of 47/316 UC pts (14.8%) underwent colectomy during the follow-up (f/u) period. The colectomy distribution was: TPC-IPAA 60%, SC-ileostomy 5%, TPC-ileostomy 33%, and PC 2%. Within the first 2 yrs of f/u, a variety of complications were observed, including (rate/1,000 pt-yrs): wound infection (204.9), anastomotic leak (56.9), fistula (22.8), abscess (68.3), small bowel obstruction (148.0), anastomotic stricture (56.9), ileus (11.4), pouchitis (148.0), and stomal problems (45.5). During the same period, the crude rate of infective and non-infective complications was 296 and 512 per 1000 pt-yrs, respectively. The total crude rate was 808/1000 pt-yrs. See table for cumulative risk of any complication following colectomy. Regression analysis indicated that, relative to TPC-ileostomy, IPAA patients had a 1.7 times greater risk of experiencing an infective complication (95% CI, 0.5–6.3) and a 2.4 times greater risk of experiencing a non-infective complication (95% CI, 0.98–6.1), but only the latter was of borderline significance.

**Conclusion:** In this population-based study of UC pts undergoing colectomy, a number of post-surgical complications were observed, for a crude rate of over 800 per 1,000 pt-yrs of f/u in the first 2 yrs, and a cumulative risk of 68.0% at 5 yrs. There was a borderline significant association between IPAA and time to first non-infective complication.

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### Risk Factors for Ulcerative Colitis (UC) Surgery in a Population-Based Cohort

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**Purpose:** We sought to identify clinical and demographic features influencing initial and subsequent surgery in a population-based cohort of UC.

**Methods:** Medical records of Olmsted County residents diagnosed with UC from 1970–2001 were reviewed to identify all surgeries. Colectomies were classified as: total proctocolectomy (TPC) with ileal pouch-anal anastomosis (IPAA), subtotal colectomy (SC) with ileostomy, TPC-ileostomy, and partial

Cumulative Risk of any Complication

Yr (95% CI)	Yr 1	Yr 5	Yr 10	Yr 15
TPC-IPAA	44.8 (23.4–60.7)	78.4 (53.2–90.0)	83.8 (57.8–94.6)	ND
SC-ileostomy	66.7 (0–93.3)	66.7 (0–93.3)	ND	ND
TPC-ileostomy	35.7 (5.0–56.5)	51.0 (15.5–71.6)	59.2 (21.6–78.7)	59.2 (21.6–83.8)
PC	43.1 (26.9–56.0)	68.0 (50.1–79.4)	73.8 (55.8–85.4)	73.8 (55.8–89.9)

ND, no data.



colectomy (PC). Planned 2nd-stage surgeries were excluded in counting unplanned follow-up surgeries. Cumulative incidences of initial colectomy from time of diagnosis (dx) and follow-up surgeries from time of colectomy were estimated actuarially. Proportional hazards regression was used to assess association of clinical/demographic features with time to colectomy and time to follow-up surgery (after colectomy).

**Results:** 316 UC pts (57% males) were followed for 3,698 person-yrs. Fifty-three pts (17%) had a surgery for UC, of whom 37 (70%) underwent >1 procedure. See table for cumulative risks of initial colectomy and selected subtypes. Males were more likely to undergo colectomy (hazards ratio[HR], 2.2; 95% CI, 1.1–4.1). Extensive UC was not significantly associated with colectomy (HR, 1.4; 95% CI, 0.7–2.6) relative to proctitis/left-sided UC. Use of steroids within 90 days of UC dx was strongly associated with colectomy (HR, 3.2; 95% CI, 1.6–6.5). Initial colectomy subtypes were: TPC-IPAA (62%), SC (6%), TPC-ileostomy (30%), and PC (2%). Second colectomy-related surgeries were common, including ostomy closure in 60%; this varied by colectomy type. The 10-yr cumulative risk of subsequent unplanned surgery was 44.1% overall and varied by colectomy type (see table). Those undergoing TPC-IPAA compared to TPC-ileostomy were 1.9 times more likely to have unplanned follow-up surgeries, but this difference was not significant (95% CI, 0.6–5.9).

**Conclusion:** In this population-based cohort of UC pts, the 20-yr cumulative incidence of colectomy was ~20%. Male gender and early need for corticosteroids were significantly associated with colectomy. The most common surgeries were TPC-IPAA and TPC-ileostomy, and frequent unplanned surgeries post-colectomy were observed.

	Cumulative Risks		
	IPAA	TPC-ileostomy	Total
10-yr colectomy from dx	10.7 (6.6–14.7)	4.9 (2.1–7.6)	16.6 (11.7–21.3)
20-yr colectomy from dx	12.1 (7.6–18.4)	5.9 (2.5–10.2)	19.6 (14.0–26.5)
10-yr unplanned surg from colectomy	49.7 (25.0–68.8)	34.1 (0–56.9)	44.1 (25.7–59.3)

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### Validation of an Algorithm for Predicting IBD, CD and UC in a Comprehensive Population

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**Purpose:** Prometheus has developed a novel algorithmic approach (Prometheus® IBD Serology 7) to IBD serologic marker analysis. The algorithm is a sophisticated computation in which learning statistical classifiers sequentially analyze a patient's serologic test results. The tests include assays for ASCA, anti-OmpC, anti-CBir1, and ANCA. The algorithmic analysis does not compare the patient's values to a standard reference range but rather to disease and non-disease serologic patterns. Previously we have detailed the algorithm performance in a validation cohort of 500; in this study we describe a new expanded cohort of 740 subjects which includes pediatric samples.

**Methods:** The algorithm was trained to recognize serologic patterns using a cohort of 1813 patients (including 60 pediatric samples) with confirmed diagnoses of CD (N = 646), UC (N = 431), GI disease controls (N = 366), and no disease (N = 370). The ability of the algorithm to predict CD, UC and non-IBD was tested in a validation cohort. The validation cohort consisted of 740 patients (590 ≥ 18 years and 150 < 18 years) with known

diagnoses, including CD (N = 246), UC (N = 115), GI disease controls (N = 172) and no confirmed disease (N = 207). The prevalence of IBD in the validation cohort was 49%. None of the samples used in the development of the algorithm was used for its validation.

**Results:** Performance characteristics of the algorithm are shown below. In addition ROC analysis indicates that the algorithm accurately discriminates IBD from non-IBD and CD from UC with area under the curve calculations of 0.9 for both comparison.

**Conclusion:** Algorithmic analysis of serologic marker data in a cohort of 740 subjects (including 20% pediatric patients) results in accurate predictions of CD, UC and non-IBD and discrimination between CD and UC.

Algorithm Performance Characteristic

Validation cohort (740)	IBD	CD	UC
Sensitivity	91%	87%	90%
Specificity	85%	91%	96%
Positive Predictive Value	85%	83%	81%
Negative Predictive Value	91%	93%	98%

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### Influence of Disease Duration and Severity on Inflammatory Bowel Disease Patients' Medication Preference

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**Purpose:** Inflammatory Bowel Disease (IBD) is a lifelong condition that often requires multiple medications to treat flares of disease activity and to maintain remission. The aim of this study was to investigate if a patient's disease severity and duration influenced his or her choice of medical or surgical treatment preferences, in order to better prescribe appropriate medication for maximizing compliance.

**Methods:** A comprehensive questionnaire was administered to 50 consecutive patients with a known diagnosis of IBD, visiting the Yale IBD clinic from July to November 2006. The questionnaire included demographics, disease and medication history, questions on preferences of medication types (5-aminosalicylic acid agents (5ASA), enemas, oral steroids, immunosuppressants, anti TNF agents and surgery) with reasons. The patients were divided into 2 groups based on their disease severity-mild (1–4 bowel movements/day, no urgency, rare blood, mild pain) and moderate/severe (>5 bowel movements/day with blood, urgency and interference with daily activities). The same set of patients were also divided into 2 groups based on disease duration (DD) ≤ 10 years and > 10 years.

**Results:** The questionnaire was completed by 50 patients (33 with CD and 17 with UC). The patients comprised 28 females and 22 males with a mean age of 41.52 (± 15) years and mean disease duration of 8.8 (± 9.6) years. Treatment preferences of the different groups are as follows:

Majority of the patients preferred 5ASA due to its efficacy and milder side effect profile. Surgery was the least preferred treatment modality due to side effects and cost, followed by steroids due to their side effects.

**Conclusion:** In our preliminary report, disease severity appeared to influence the choice of preferred medication, with moderate to severe disease patients preferring more aggressive treatment modality like anti TNF agents equally to 5ASA. Patients with any disease severity unanimously chose surgery as the least preferred treatment. Disease duration did not affect the preferred

Categories	Mild Disease	Moderate/Severe Disease	DD ≤ 10 yrs	DD > 10 yrs
n	39	11	36	14
Preferred Medication	5ASA (53.8%)	5ASA (36.4%), antiTNF(36.4%)	5ASA (50%)	5ASA (50%)
Disfavored Medication	Surgery (43.6%)	Surgery (36.4%)	Surgery (38.9%), Oral Steroids (38.9%)	Surgery (50%)

medication with 5ASA being the top choice of treatment, but patients with shorter disease duration did not prefer oral steroids equally to surgery.

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### Merkel Cell Carcinoma Arising after Therapy with Azathioprine for Ulcerative Colitis

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**Purpose:** 1) To recognize an atypical skin lesion in the context of immunosuppression with azathioprine 2) To describe the clinical features, treatment and recommendations for Merkel Cell Carcinoma 3) To illustrate the increased risk of malignancy among patients with inflammatory bowel disease treated with immunosuppression.

We report a case of a 78 year old male with Ulcerative Colitis (UC) maintained on azathioprine and asacol. His clinical course complicated by development of Cutaneous Merkel Cell Carcinoma (MCC) of the right thigh. After 18 months, his disease metastasized to the pelvic lymph nodes. Patient underwent wide local excision with dissection of lymphatics, followed by pelvic lymphadenectomy with chemotherapy and radiation. Pathophysiology revealed clusters of neoplastic cells consistent with MCC. Azathioprine was discontinued with subsequent exacerbation of UC. The patient presented to our institution with severe colitis after completing radiation therapy for Metastatic MCC with diagnoses of UC exacerbation and Cytomegalovirus Colitis.

Physical Exam revealed well healed surgical scars in the right lower quadrant and a right thigh, without any abdominal tenderness or masses. Rectal exam was grossly positive for blood.

MCC is rare, aggressive, cutaneous malignant tumor with a high incidence of local-regional recurrence, and distant metastases. The tumor arises from Merkel cells in the basal layer of epidermis and hair follicles. It is firm, painless, flesh colored or erythematous, noted on the head, neck, extremities and trunk. Like other skin malignancies, it occurs in areas of greatest sun exposure. Treatment involves; wide local excision, regional lymphadenectomy, chemotherapy and radiation.

Review of literature proposed several mechanisms to explain the increase risk of MCC, as well as other malignancies associated with azathioprine use. Foremost, since azathioprine acts directly on disruption of cell-mediated immunity by inhibiting purine synthesis (cell division), it can increase the growth of neoplasm by compromising immune system surveillance. Secondly, azathioprine is a derivative of the purine analogue 6 mercapto-purine and via its metabolite 6 thioguanine which is incorporated into DNA, can lead to disruption of DNA synthesis. Lastly, azathioprine may potentiate the effects of environmental carcinogens such as ultraviolet radiation by increasing the number of DNA exchanges between sister chromatids leading to gross chromatic aberrations and thus chromosome damage.

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ABSTRACT WITHDRAWN

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### The Impact of Ulcerative Colitis on Patients' Lives Compared with Other Chronic Diseases: A Patient Survey

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**Purpose:** To understand patients' perspectives of the impact that ulcerative colitis (UC) has on their lives and to compare this impact with that of other chronic conditions.

**Methods:** An internet survey covering a variety of disease-impact indices was conducted in patients with UC, rheumatoid arthritis (RA), asthma or migraine. Differences in responses between patient populations were considered significant if  $P < 0.05$ .

**Results:** Overall, 451 patients with UC (20% mild, 63% moderate, 13% severe [as informed by their physician]), 309 with RA, 305 with asthma and 305 with migraine were included in the survey. Patients with UC reported a mean of 8 flare-ups/year (normal disease and flare-ups were not pre-defined, and thus open to patient interpretation). Significantly more patients with UC (81%) believed the number of flare-ups they experienced was 'normal', compared with patients with migraine (64%) or asthma (75%). Most patients with UC considered not feeling well had become normal (73%) and it was difficult to lead a normal life (62%). These numbers were significantly higher than the corresponding values for patients with asthma (43% and 33%) or migraine (64% and 59%, respectively). Significantly more patients with UC thought their condition was controlling their lives (53%) compared with patients with RA (44%), asthma (19%) or migraine (37%). Patients with UC were also significantly more likely to: worry about the long-term effects (84%); consider their condition was making life more stressful (82%); and feel depressed (62%) and embarrassed (70%) than patients with the other chronic conditions.

**Conclusion:** UC has a substantial detrimental effect on patients' lives. Compared with other chronic diseases, the impact is more severe, particularly with regard to the psychological burden.

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**Inflammatory Bowel Disease in the Setting of Autoimmune Pancreatitis**  
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**Purpose:** Though there have been scattered case reports of inflammatory bowel disease (IBD) occurring in patients with autoimmune pancreatitis (AIP), the prevalence of IBD in patients with AIP is unknown. We sought to better characterize the putative association between the conditions.

**Methods:** Medical records of 71 patients with AIP meeting the HISORT criteria (*Clin Gastroenterol Hepatol* 2006;4:1010–1016) were reviewed to identify patients with endoscopic and biopsy evidence of IBD. Clinical features and outcomes were described. Colon samples were immunostained to identify IgG4 positive cells.

**Results:** 4 patients with AIP (5.6%) had a diagnosis of IBD; 3 had ulcerative colitis (UC) and 1 had Crohn's disease (CD). Diagnosis of IBD preceded that of AIP in 3 patients, and was simultaneous in 1. Serum IgG4 was elevated in 1 of 2 patients with AIP and IBD, compared to 31 of 44 in those with AIP alone. Only 1 of 4 patients with AIP and IBD had a positive p-ANCA. Primary sclerosing cholangitis-like intra-hepatic biliary strictures were seen in 1 of 4 patients with AIP and IBD. 2 patients treated for AIP with a standard prednisone taper had recurrence of AIP, with 1 requiring 6-mercaptopurine for long-term steroid-sparing treatment. The other 2 patients underwent Whipple procedures, with 1 recurrence of AIP. All 3 UC patients presented with extensive colitis, with total colectomy for refractory colitis necessary in 2 of 3 patients. Colon samples from 1 patient with UC and 1 patient with CD were available for review. 10 IgG4 positive cells/high power field were noted on the colon sample from the patient with UC; none were seen on the CD sample.

**Conclusion:** As recognition of AIP increases, several important clinical associations become apparent, including the relationship between AIP and IBD. Almost 6% of patients in our cohort of 71 patients with proven AIP had a diagnosis of IBD, compared to a prevalence of approximately 0.4 – 0.5% in the general population, potentially implying a 12-fold to 15-fold increase in risk. Interestingly, all 3 UC-AIP patients presented with extensive colitis; two with refractory colitis requiring total colectomy. The finding of IgG4 positive cells on colon biopsy suggests that IBD may represent an extra pancreatic manifestation of AIP. Further studies are needed to determine if IBD is an extra-pancreatic manifestation of AIP or an associated disease.

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#### Patient and Physician Perceptions on Living with Ulcerative Colitis: Results from Two Internet Surveys

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**Purpose:** To understand how the perception of the impact of ulcerative colitis (UC) on patients' lives differs between patients and gastroenterologists.

**Methods:** Two national internet surveys were conducted: one in patients with UC and one in gastroenterologists. Here we present selected results from these surveys. Patients with a history of colectomy were excluded.

**Results:** 451 patients with UC (20% mild, 63% moderate, 13% severe [as informed by their physician]) and 300 gastroenterologists (unassociated with the patients) were included in the surveys. In total, 36% of patients reported having  $\geq 6$  flares per year (subjective self-definition). This number exceeded gastroenterologists' expectations for a patient population with this distribution of disease severities. When patients were asked what being in remission meant to them, 44% believed it meant living with UC symptoms, but managing life without interruption. Although ~55% of patients reported being prescribed 5-aminosalicylic acid (5-ASA) therapy, the gastroenterologists reported prescribing 5-ASA therapy to 87% of their patients. Both patients and gastroenterologists reported that managing UC medication is a struggle for patients (49 and 41%) and that it is difficult for patients to take medication as prescribed every day (42 and 90%). Indeed, 46% of patients admitted to not taking all of their medication in the past week, while gastroenterologists believed that 41% of their patients were not adherent.

**Conclusion:** These surveys show important disparities between how patients and gastroenterologists perceive the impact of living with UC. Results suggest that many patients have adapted to live with their symptoms rather than acting to optimize therapy and compliance. Improvements in management strategies, education, and communication among patients and gastroenterologists are necessary.

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#### Long-Term Safety of 5-Aminosalicylates (Mesalamine) in the Treatment of Inflammatory Bowel Disease

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Incidence of Renal Insufficiency and Leukopenia with 5-ASA Medications

	Number of patients (N)	Average daily mesalamine dose, gm/day (SEM)	Average duration of exposure to mesalamine, months (SEM)
Ulcerative Colitis	95	3.11 (0.13)	43.08 (4.52)
Patients with Cr $\geq 1.2$ mg/dl	6	2.53 (0.40)	52.83 (31.53)
Patients with WBC $\leq 4K$	7	2.57 (0.39)	81.29 (20.40)
	(4/7 were on 6MP)		
Crohn's Disease	110	3.17 (0.09)	35.77 (3.41)
Patients with Cr $\geq 1.2$ mg/dl	6	2.89 (0.29)	24.33 (6.76)
Patients with WBC $\leq 4K$	9	3.26 (0.22)	53.22 (10.67)
	(8/9 were on 6MP)		
Indeterminate Colitis	9	2.98 (0.28)	21.67 (7.49)
Patients with Cr $\geq 1.2$ mg/dl	0	Number of patients with WBC $\leq 4K$	Number of patients with Cr $\geq 1.2$ mg/dl
Patients with WBC $\leq 4K$	0	16	12

**Purpose:** The purpose of this study was to evaluate the safety of high dose, chronic use of 5-ASAs and identify any adverse events focusing on nephrotoxicity and hematologic side-effects.

**Methods:** We retrospectively reviewed 214 charts of patients with IBD. For each patient we calculated the equivalent mesalamine dose using appropriate conversion formulas, duration of exposure to the medication and adverse events during the course of their follow up.

**Results:** Of the 214 patients, 134 patients were exposed to 5-ASAs for over 12 months. 198/214 patients (92%) were treated with an average mesalamine dose greater than the FDA approved maintenance dosage.

Of the 12 patients with elevated serum creatinine concentrations, 4 were on no other medications and had no concomitant illnesses accounting for renal disease. Their glomerular filtration rates, as calculated by the Modification of Diet in Renal Disease study equation, ranged from 69.24 to 85.06 ml/min/1.73 m<sup>2</sup>, implying a mild reduction or stage II kidney disease. Of the 16 patients with leukopenia, 4 were only on 5-ASA medications, 2 on sulfasalazine and the other 2 on mesalamine. These findings were independent of the average daily 5-ASA dose or duration of exposure.

**Conclusion:** This is the first report regarding the long-term safety of 5-ASA medications. Overall, these medications are safe at an average dose up to 3.17 gm/day over a period of up to 80 months. A small percentage of our patients had evidence of Stage II kidney disease and leukopenia of unknown etiology. Periodic monitoring of serum creatinine and CBC are warranted during long-term treatment with 5-ASA medications.

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### Observations on a Large Sample Set Using Serologic Markers To Predict Inflammatory Bowel Disease, Ulcerative Colitis (UC), and Crohn's (CD)

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**Purpose:** Over the past 10 years serological tests have been developed to predict IBD and multiple serologic markers utilized in this process contribute to the complexity of the analysis. Prometheus has developed an algorithmic method to aid in resolving this complexity and to predict IBD. This observational study presents data on the use of this algorithm in a large cohort of samples.

**Methods:** Over an extended period of time 47,017 samples were received at Prometheus for IBD testing with unknown clinical diagnosis. All samples were tested for several serological markers including ANCA, ASCA, Anti-OmpC, and Anti-CBir-1.

**Results:** The Prometheus smart diagnostic algorithm predicted CD in 34% (16,058), UC in 11% (4,973), and non-IBD in 55% (25,986) of the samples received. In order to investigate the contribution of individual markers to the prediction, cut off analysis was performed for each of the 3 categories of predictions. In the cut off analysis, a marker was positive if its value was 2 standard deviations above a mean value calculated for non-disease controls. For CD a cut-off analysis was done using the following 4 markers: ASCA, Anti-CBir-1, Anti-OmpC and ANCA. Of the 16,058 CD predictions 86%, 28%, 14%, and 6% were positive for one, two, three, or 4 markers respectively. In this analysis the predominant single marker was Anti-CBir-1 followed by ASCA. In addition, 14% of the CD predicted samples had all markers below cut-offs.

For UC a cut-off analysis was done using the same markers as were used for the CD analysis. Of the 4,973 UC predictions 92%, 26%, 8%, and 1% were positive for one, two, three, or 4 markers respectively. In this analysis the most predominant marker was ANCA followed by Anti-OmpC. In addition, 8% of the UC predicted samples had all markers below cut-offs.

For the non IBD category of prediction, 64% of all markers were below cut off and 31% of the predictions have one marker above cut off and in this analysis the predominant single marker was Anti-CBir-1 followed by Anti-OmpC.

**Conclusion:** These data are consistent with published frequency of the four previously identified serologic markers in IBD and indicate that IBD is a

very heterogeneous and complex disease. The number of markers required to predict disease and the complexity of marker patterns is best served by a sophisticated algorithmic approach. Results also indicate that a significant number of patients predicted to have either CD or UC have serology markers below the normal cut-offs.

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### Compassionate Use of Certolizumab Pegol in Patients with Crohn's Disease for Whom Treatment with One or Two Anti-TNFs Failed

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**Purpose:** The efficacy and safety of certolizumab pegol (CZP), the first Fc-free PEGylated Fab' anti TNF, in Crohn's disease (CD) were shown in large Phase III trials. A compassionate-use program (COMPAS) allows physicians to use CZP in resistant cases. COMPAS provides the first data for CZP effectiveness in CD in clinical practice.

**Methods:** COMPAS includes patients (pts) with CD for whom approved conservative therapies had failed. The recommended dose regimen is that on the submitted label (400 mg sc induction at Weeks (Wks) 0, 2, and 4, then 400 mg sc maintenance every 4 wks). Treatment was deemed effective if there was a clinical response (clinical improvement satisfactory to both pt and investigator, with the pt remaining on treatment) and no adverse events (AEs) leading to withdrawal.

**Results:** By May 2007, COMPAS involved 182 gastroenterologists in 18 countries, with requests received from 284 physicians. Drug-release criteria were met by 216 pts and 160 (65% female; mean age 37 years) had been treated. Most pts were receiving immunosuppressants and/or corticosteroids at baseline; 17 pts had fistulas; 114 pts (71.2%) are ongoing. At the cut-off date, median exposure is 86 days (all pts) and 104 days (ongoing pts). At Wk 8, 79/160 pts (49.3%) responded. Of these, 59 (36.8%) were still in response after 8 wks; 31 (52.5%) remained on treatment at Wk 20, 11 (18.6%) at Wk 32, and 8 (13.6%) at Wk 40. No pts had responded to infliximab; 39 pts had not responded to either infliximab or adalimumab. Of the 39 pts, 21 (53.8%) responded to CZP induction and reached the maintenance phase. AEs occurred in 22 pts, with 16 serious AEs that included small intestine carcinoma (history of severe CD/successive immunosuppressives/5 months' therapy), acute left cardiac insufficiency and renal failure (obesity and family history of myocardial infarction/2 wks' therapy), and acute urticaria (pt had similar reactions to previous anti-TNF therapies).

**Conclusion:** COMPAS offers a first chance for pts with CD to receive CZP in real-life conditions. Despite only pts with severe and resistant disease being included, the clinical efficacy and safety profiles of CZP were similar to those in controlled clinical trials.

This research was funded by UCB.

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### Impact of Crohn's Disease Severity on Healthcare Costs and Utilization

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**Purpose:** We quantified the impact of disease severity on healthcare utilization and cost in patients (pts) with Crohn's disease (CD) compared with nonCD controls.

Annualized Mean healthcare Utilization and Costs

Category	Controls N = 2972	R N = 729	M N = 711	SDRS N = 780	SDD N = 514	SDRF N = 238	CD (all) N = 2972
Mean healthcare claims/100 pt-years							
Emergency room visits	26	47	59	94	74	84	70
Physician visits	500	1030	970	1270	1230	1270	1130
GI procedures	487	1432	1163	1744	1742	1989	1548
Hospitalizations	8	47	26	58	57	49	47
Mean healthcare costs (US \$/pt-years)							
Emergency room visits	76	157	264	319	223	343	251
Physician visits	306	702	680	908	934	900	807
GI procedures	350	1833	1513	2088	2113	10,491	2565
Hospitalizations	691	6107	3175	6172	6720	5196	5456

**Methods:** Patients from PharMetrics, a US claims database (Jan 2000–June 2005), were included with  $\geq 3$  distinct claims with a CD diagnosis or  $\geq 2$  claims including  $\geq 1$  diagnosis by a gastroenterologist. Cases were matched (1:1) to controls by age, gender, region, enrollment year, length of enrollment, and health plan. A treatment algorithm defined disease severity as: remission (R); mild disease (M); severe disease drug-responsive (SDRS); severe disease drug-dependent (SDD); severe disease drug-refractory (SDRF). Differences in annualized utilization (mean number of outpatient care visits, gastrointestinal [GI] procedures, and hospitalizations per 100 pt-years) and payor-related costs (2005 US\$/pt-year) were analyzed using Wilcoxon signed-rank tests.

**Results:** The analysis included 2972 pts with CD (54% female). Main drivers for outpatient care were GI procedures and physician visits. Most severe disease required more outpatient care. Hospitalization and GI procedures were the highest costs in the CD group; in the SDRF group, GI procedure costs were substantially higher than for all other severity groups.

**Conclusion:** More severe disease was associated with greater healthcare costs, with hospitalization as the main cost. Regardless of severity, all CD pts had higher utilization and costs compared with controls. Costs were comparatively high in the remission group, indicating a high demand for healthcare services despite no/low medication use.

This research was funded by UCB.

Correlations between changes in baseline utility scores and in Inflammatory Bowel Disease Questionnaire (IBDQ) scores at Wk 26 were evaluated using Kendall's tau coefficients.

**Results:** Mean utility scores increased by 34.3% ( $P < 0.001$ ) during induction with CZP. During maintenance therapy, the mean utility score in the CZP group was 8.6% ( $P = 0.007$ ), 4.2% ( $P = 0.064$ ), and 7.0% ( $P = 0.002$ ) higher than the mean utility score in the PBO group at Wks 16, 26 and at the last/withdrawal visit, respectively. Gains in utility scores were associated with improvements in IBDQ scores (positive Kendall's tau values,  $P < 0.001$ ); correlations coefficients ranged from 0.34 (social function) to 0.42 (global score).

**Conclusion:** CZP maintained improvements in EQ-5D-derived utility scores observed after CZP induction significantly better than PBO. These improvements were associated with a better health-related quality of life for CD patients.<sup>4</sup>

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### Changes in Utility Scores of Patients with Active Crohn's Disease after Certolizumab Pegol 400 mg Induction and Maintenance (PRECiSE 2)

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**Purpose:** PRECiSE 2 demonstrated the efficacy and safety of certolizumab pegol (CZP), a PEGylated Fc-free Fab' anti-TNF $\alpha$ , in Crohn's disease (CD).<sup>1</sup> Patient-reported health status was captured using the self-administered EQ-5D questionnaire, which assesses mobility, self-care, usual activities, pain/discomfort and anxiety/depression on a 3-point scale (no/some/extreme problems).<sup>2</sup> This analysis evaluated the effect of CZP on the utility scores of CD patients in PRECiSE 2.

**Methods:** Patients with active CD who responded to induction therapy (CZP 400 mg, Weeks [Wks] 0, 2, and 4) at Wk 6 (64.1%) were randomized to receive CZP 400 mg (N = 215) or placebo (PBO, N = 210) every 4 wks, Wks 8–24. The EQ-5D was completed at Wks 0, 6, 16, and 26, and at withdrawal. Responses were converted to utility scores,<sup>3</sup> i.e. patients' rating of their current health states from -0.59 (worst state imaginable) to 1.00 (best).

Mean utility scores at Wks 0 and 6 were compared using a paired t-test; scores were compared between treatment groups at each timepoint using the Wilcoxon test.

## 1000

### Evaluation of Ten Cytokines in Response to Treatment of Active UC

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**Purpose:** There exists no reliable blood biomarker of the activity of UC. Although CRP is widely used in clinical practice, it has limitations. Cytokines that reflect Th1 and Th2 activity are other potential candidates. This pilot study examines the relationship between clinical criteria of activity and the cytokine levels in patients with active UC.

**Methods:** Samples from 21 patients with moderately active UC (Mayo score 7–11) were recruited after informed consent. Blood samples were taken before and after treatment from each patient. Samples were analysed for concentrations of IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, IL-12, IL-13, IFN- $\gamma$  and TNF- $\alpha$  using a manufacturer defined protocol. Logistic regression was used to model post-treatment Mayo scores as a function of baseline cytokine concentration and the change in cytokine concentration after treatment. Cytokine concentration was correlated with treatment outcome, symptoms (stool frequency and rectal bleeding), endoscopic appearance, extent of UC and between biomarkers.

**Results:** The model identified a relationship between baseline [IL-5], [IL-8] and [IL-10] and response to treatment, ( $\beta$ IL-5 = -1.1,  $P = 0.142$ ,  $\beta$ IL-8 = -0.07,  $P = 0.070$ ,  $\beta$ IL-10 = -0.18,  $P = 0.034$ ), but its predictive ability was weak. Higher baseline [IL-5] and [IL-8] and lower [IL-10] predicted

lower post-treatment Mayo scores. The relationship was strongly influenced by data outliers. Modelling the change in cytokine concentration identified only  $\Delta$ [IL-2] as potentially associated with treatment outcome ( $P = 0.0003$ ). Positive  $\Delta$ [IL-2] correlated with higher post treatment Mayo scores. The relationship was not robust and had weak predictive ability. Concentrations of IL-2, IL-4, IL-12, IFN- $\gamma$  and TNF- $\alpha$  all correlated with each other (all  $P < 0.0001$ ), but neither individually nor in combination with treatment outcome, clinical or endoscopic criteria of response.

**Conclusion:** Neither baseline nor changes in cytokine concentrations, either singly or in combination, were sufficiently robust to predict treatment response in this pilot study. Nevertheless, the combination of baseline [IL-5], [IL-8] and [IL-10], or change in [IL-2] are worth exploring in larger studies. Multiplex biomarker analysis has the potential for evaluating host response to the disease activity. Clear correlations between IL-2, IL-4, IL12, IFN- $\gamma$  and TNF- $\alpha$  in patients with active UC support the concept of a balance between Th1/Th2 responses in acute colitis.

## 1001

### Evaluation of the Combination of Fecal Lactoferrin and Fecal Anti-Saccharomyces Cerevisiae Antibodies To Detect Active Crohn's Disease

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**Purpose:** Prior studies of a quantitative assay for fecal lactoferrin showed high sensitivity and specificity in detecting intestinal inflammation in inflammatory bowel disease (IBD). Prior studies have indicated that an assay to detect fecal antibodies to *Saccharomyces cerevisiae* (ASCA) may be able to identify patients (pts) with Crohn's disease (CD). We sought to determine the diagnostic utility of a combined analysis to detect both fecal lactoferrin and fecal ASCA in pts evaluated at an IBD clinic.

**Methods:** Between 3/04 and 10/06, pts with known or suspected CD who were undergoing evaluation with colonoscopy +/- small bowel x-ray were offered enrollment. Study subjects provided stool and serum samples within 72 hrs of colonoscopy and these were sent for analysis (quantitative enzyme-linked immunoassay [EIA] for fecal lactoferrin, qualitative EIA for both fecal and serum ASCA, and INOVA serum ASCA IgG). The reference standard was physician global assessment based on colonoscopy, biopsy, and (if available) small bowel x-ray (CT enterography or small bowel follow-through).

**Results:** A total of 69 pts were enrolled (39 active CD, 12 inactive CD, 5 active ulcerative [UC] or indeterminate colitis[IC], and 13 non-IBD conditions). In the active CD group, 6 did not submit stool samples and 3 did not submit serum. Three non-IBD pts and 1 UC/IC pt did not submit serum. See table for comparisons of fecal lactoferrin and fecal/serum ASCA. Fecal lactoferrin was elevated in 33 of 38 pts with active IBD (87%) vs. 17% of inactive CD and 38% non-IBD miscellaneous. Fecal ASCA was detected in both active and inactive CD.

**Conclusion:** Fecal lactoferrin distinguishes active IBD from inactive IBD and miscellaneous GI disorders. Fecal ASCA is present in the majority of CD pts and may aid in distinguishing CD from non-IBD; however, additional studies using a larger number of active UC pts are needed to evaluate the role of fecal ASCA to differentiate UC from CD.

	Active CD	Inactive CD	UC/IC	Non-IBD
Elevated fecal lactoferrin, n (%)	29 (88%)	2 (17%)	4 (80%)	5 (38%)
Fecal ASCA, n (%)	21 (64%)	6 (50%)	4 (80%)	2 (15%)
Serum ASCA	23 (64%)	7 (58%)	0	0
INOVA ASCA	30 (83%)	6 (50%)	1 (25%)	1 (10%)
Mean (SD) lactoferrin ug/mL	1012 (1689)	6.5 (11.2)	6.5 (11.2)	14.5 (21.1)

## 1002

### Willingness of Individuals with IBD To Use Complementary and Alternative Medicine

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**Purpose:** Interventions that are not based on the standard therapeutic approaches of western medicine are categorized as techniques of Complementary and Alternative Medicine (CAM). However, almost half (3 billion people) of the world's population rely on their traditional CAM systems as their primary form of health care. Even 30% of Americans use CAM for their ailments. In this study we evaluated the willingness of IBD subjects to use CAM and their experiences with these therapeutic modalities.

**Methods:** We had subjects with ulcerative colitis (UC) and Crohn's disease (CD) complete questionnaires that assessed disease severity, disease duration, and respondents' opinions and experiences with various CAM techniques including acupuncture, western herbs, Chinese medicine, Ayurvedic medicine, probiotics, vitamins and minerals, aromatherapy, colon cleansing, hypnosis, and nutritional supplementations. The subjects were also asked about their views on the role of diet and type of food on the course of their disease.

**Results:** We recruited 53 cases of IBD (16 UC and 37 CD). Most UC subjects (69%) and about half of CD subjects (49%) thought CAM could be beneficial for their IBD and 44% & 32%, respectively, were currently using CAM remedies. Among IBD subjects only 2% thought that alternative medicine is not effective, 28% believed that this approach is quite potent and effective, 56% were unsure, and 7% would never use it without their doctor's advice. Many subjects were willing to try different CAM techniques including acupuncture (55%), western herbs (57%), Chinese medicine (57%), Ayurvedic medicine (53%), probiotics (53%), vitamins and minerals (70%), aromatherapy (47%), colon cleansing (28%), hypnosis (38%) and nutritional supplementations (70%). Also, 70% of IBD subjects believed that diet affects their disease activity. There were no significant differences between type of IBD (UC vs. CD), disease severity and duration in their responses to these questions.

**Conclusion:** Prior studies showed that IBD subjects use CAM more than subjects with other GI ailments in the US (30% vs. 15%). Our study showed that 32–44% of IBD subject are currently using CAM and one third to one half are willing to try it. More than half of cases were open to the idea of using CAM. Also, more than two thirds of IBD subjects thought diet affected disease activity. Thus, we as physicians should address the issue of CAM use very seriously when we approach our patients' concerns in our clinical encounters.

## 1003

### Experience with Wireless Capsule Endoscopy in the Evaluation of Patients with Crohn's Disease

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**Purpose:** The diagnosis of Crohn's disease (CD) is often difficult and many patients remain in the category of "indeterminate colitis" or "inflammatory bowel disease type unclassified" (IBDU). Traditionally, suspected CD has

been evaluated with small bowel series and push enteroscopy where sedation is required and only a part of small bowel is visualized (up to 120 cm beyond the ligament of Trietz).

The introduction of WCE allows painless visualization of the entire small bowel mucosa and also helps in the early detection of mucosal lesions/ulcerations in patients with suspected CD/IBDU. WCE has been shown by meta-analysis to be a more sensitive method to investigate patients for small bowel CD, with an incremental yield above 30% versus other imaging modalities (Leighton et al. *Inflammatory Bowel Dis.* 2007;13:331–7).

**Aim:** The aim of this study is to present data based on our experience with WCE in the evaluation of suspected CD and its utility in establishing a diagnosis in patients with “indeterminate colitis”/IBDU.

**Methods:** In this retrospective study, data is from WCE performed during the last 5-year period (2002–2007). Patients with complaints of unexplained abdominal pain and/or chronic diarrhea underwent WCE for the evaluation of suspected CD. The diagnosis of CD was made if WCE showed > 3 ulcerations (linear/aphthous). (Maunoury et al. *Inflammatory Bowel Dis.* 2007;13:152–5).

**Results:** Total no. of WCE: 652 (Males = 311, Females = 341) WCE performed for suspected CD = 68/652 cases (10%) Diagnosis of CD was made = 18/68 cases (26%) CD was diagnosed in patients with past history Ulcerative colitis (UC) with total colectomy = 3 cases.

Retained capsule in small bowel due to a stricture secondary to CD = 1 case.

**Conclusion:** 1) WCE plays a major role in the diagnosis of CD especially in cases of indeterminate colitis/IBDU. 2) In our observation, some patients who have undergone total colectomy for the presumptive diagnosis of UC showed small bowel lesions suggestive of CD. This raises a need of evaluating small bowel mucosa by WCE prior to elective total colectomy for UC. It may also be appropriate to evaluate the small bowel mucosa with WCE in all patients with suspected UC. 3) Complications of WCE in patients with CD although rare, include capsule retention at the stricture sites. The new AGILE patency capsule (Given Imaging) can diminish this in high-risk patients.

## 1004

### Hospitalization Rates for Crohn's Disease Patients in Olmsted County, Minnesota, in the Pre-Biologic Era

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**Purpose:** Inpatient hospitalization is a major component of health care resource consumption for patients (pts) with Crohn's disease (CD). However, there are limited data on annual hospitalization rates for CD pts not treated with anti-tumor necrosis factor (TNF) therapy. We sought to estimate the historical hospitalization rates for a population-based cohort of CD pts from Olmsted County, Minnesota, in the pre-biologic era.

**Methods:** Previously identified county residents diagnosed with CD between January 1970 and June 1997 were included in the analysis and were followed until June 1997. Medical records were abstracted for all CD-related hospitalizations, which were classified as surgical or medical. For pts who were hospitalized at the time of CD diagnosis (N = 73), the initial hospitalization was not included in estimates. Crude incidence rates over the entire follow-up period and the first year after diagnosis of CD were calculated.

**Results:** A total of 211 patients with CD were included and were followed for 2,247 pt-yrs. Median age at diagnosis was 29 years (range, 8.4–88.5), and 51% were female. One hundred twenty pts (56.9%) had at least one CD-related hospitalization (median per pt, 2 [range, 1–22]). Excluding the 73 initial hospitalizations at time of diagnosis, the patients experienced 437 hospitalizations (194 per 1000 pt-yrs), including 165 hospitalizations with inpatient surgeries (73 per 1000 pt-yrs).

**Conclusion:** Before 1998, when biologics such as TNF antagonists were not yet available, the crude rate of CD-related hospitalizations was relatively high. The crude hospitalization rate in the first yr after CD diagnosis was over twice as high as the overall rate. These data provide a baseline reference for comparison to gauge the impact of anti-TNF therapy on hospitalization

rates in patients with CD. Therapies that reduce the hospitalization risk may provide substantial benefits to patients with CD.

CD-Related Hospitalizations in Olmsted County, 1970–97			
	Medical	Surgical	Total
Pts With At Least 1 Hospitalization, n (%)	97 (46.0%)	89 (42.2%)	120 (56.9%)
Hospitalizations, n (Crude Rate Per 1,000 Pt-Yrs)*	272 (121)	165 (73)	437 (194)
Hospitalizations In First Yr After Diagnosis, n (Crude Rate Per 1,000 Pt-Yrs)*	55 (277)	39 (197)	94 (474)

\*Excludes initial hospitalization if hospitalized at diagnosis.

## 1005

### ABSTRACT WITHDRAWN

## 1006

### A Prospective, Controlled Longitudinal Study of the Effects of Oral Steroids at 3 and 6 Months on Bone Mineral Density (BMD) in Patients with IBD

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**Purpose:** Patients with IBD are at risk for steroid induced BMD loss. However, the duration of prednisone use required to produce bone loss, and the natural history of BMD after cessation of prednisone is not well described in IBD. The objective of this prospective study is to determine the rate and course of bone loss at 3 and 6 months patients in treated with prednisone (Pred), compared to a control group matched for disease activity, not treated with prednisone (non-P).

**Methods:** Pred patients (N = 22) underwent baseline DEXA to determine BMD at the lumbar sacral spine (LSS), and bilateral hips, and were compared to non-P patients (N = 18) with active disease; all patients underwent serial DEXA measurements at 3 and 6 months. All patients were treated empirically with oral calcium 1500 mg/d and vitamin D 600 u/d. Baseline disease activity was assessed using the modified Mayo score for UC, and the Harvey Bradshaw Index for CD.

**Results:** 21 UC patients and 19 CD patients, 28 males and 12 females were studied. There were no demographic differences or baseline risk factors between groups. The proportion of patients with osteoporosis at baseline were similar in the Pred and non-P groups (11.1% vs. 9.1%). The decline in mean t scores at 3 months, compared to baseline, was greater in the Pred group at the LSS, compared to non-P (-0.23 vs. -0.07), as well as at the hip (-0.23 vs. 0). There was no further decline in mean t scores between 3 and 6 months at either the LSS or hip in either the Pred or non-P group. At 3 months, 7 of 22 (32%) patients in the Pred group had >5% decline in BMD at the LSS; and 3 of 22 (14%) in the Pred group had a >5% decline in BMD at the hip. At 6 months no additional patients in the Pred group developed >5% BMD loss, and 3 of 22 reverted to <5% BMD loss at the LSS. No additional Pred patients had > 5% BMD loss at the hip.

**Conclusion:** A 3 month course of prednisone led to a greater decline in mean t scores at both the LSS and hip than in control patients by 3 months. However, in this group of patients who had discontinuation of prednisone by 3 months, and maintained on calcium and Vitamin D supplementation, there was no additional loss in BMD at the hip and a small number of patients had improvement at the LSS. A short course of prednisone, therefore did not lead to progressive bone loss beyond the duration of its use.

## 1007

### Infliximab Therapy Is Associated with Unexpected Weight Gain in Patients with Crohn's Disease as Compared to Those with Rheumatoid Arthritis

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**Purpose:** Obesity has reached epidemic proportions in the United States with approximately 31% of the population having a BMI > 30 and concern stems from the multitude of health issues associated with this condition. Crohn's disease patients often battle weight loss and anorexia, but anecdotally there appears to be significant weight gain associated with treatment of refractory CD patients with infliximab therapy, beyond that expected by improved nutritional status alone. Our purpose is to determine if infliximab therapy in patients with refractory CD is associated with significant weight gain that may change the long-term management of these patients.

**Methods:** The study is a single center retrospective chart review. IRB approval was obtained and a pharmacy list generated of patient receiving infliximab infusions from January 2002 to August 2006 (N = 394). The charts of 92 Crohn's patients and 51 rheumatoid arthritis patients that met the inclusion criteria were reviewed. Statistical analysis was made using SAS8.2.

**Results:** The mean weight gain for the CD patients was 4.97 kg compared to the mean weight gain for patients with RA of 1.1 kg ( $P < .0049$ ). Patients treated for "fistulous disease" (N = 34) had a weight gain of 6.2 kg compared to those treated for "luminal disease" (N = 58), who experienced a 4.4 kg weight gain. ( $P = .2166$ ) Chronic steroid use, smoking status, baseline BMI and baseline Harvey Bradshaw Index were not found to significantly influence weight gain in these patients.

**Conclusion:** Weight gain with infliximab therapy is more common in patients with Crohn's disease than in patients with rheumatoid arthritis. There

was no significant difference in weight gain between patients treated for fistulous or luminal disease. These findings together suggest that the weight gain seen is not totally related to increase in nutrient absorption by improving luminal disease activity. The findings of significant weight gain and increased serum leptin levels in Crohn's patients on infliximab therapy for 4 weeks in a small prospective study conducted by Franchimont et al (2005) support this conclusion. The consistent findings of significant weight gain underscore the need for a larger prospective study to try to elucidate the cause of this weight gain and the role of leptin. The absence of weight gain in patients with RA may provide important clues to the mechanism of action of this effect.

## 1008

### Prevalence of Cytomegalovirus and Epstein Barr Virus in Inflamed Colon Tissue of Patients with Mild to Moderate Inflammatory Bowel Disease – Preliminary Results

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**Purpose:** Cytomegalovirus (CMV) infection and Epstein Barr virus (EBV) DNA have been detected in colon tissue of patients with severe steroid refractory inflammatory bowel disease (IBD). However, the prevalence of CMV and EBV infection in colon tissue from patients with less severe IBD is not known. We aimed to evaluate the prevalence of CMV and EBV infection in colon tissue of patients with mild to moderate IBD as compared to their prevalence in normal colon mucosa of non IBD patients, non inflamed colon mucosa in same IBD patients and inflamed mucosa in patients with other inflammatory diseases of the colon.

**Methods:** Consecutive colonic tissue biopsy specimens were taken through colonoscopy from 41 patients with quiescent and mild to moderate IBD (N = 30 with ulcerative colitis and N = 11 with Crohn's colitis) and from 49 control patients; N = 6 with colitis from other inflammatory conditions of the colon and N = 43 from patients without IBD undergoing colonoscopy for purposes of colorectal cancer screening. Detection of CMV and EBV infection from tissue biopsies was performed using quantitative PCR and immunohistochemistry or *in-situ* hybridization.

**Results:** Prevalence of CMV and EBV in inflamed mucosa of quiescent and mild-moderate IBD is 8.1% and 11.4%, respectively. CMV was significantly more prevalent in inflamed mucosa of UC patients compared to healthy controls (11.5% vs 0%;  $P < 0.05$ ). EBV is significantly more prevalent in inflamed mucosa of IBD and ulcerative colitis patients as compared to healthy controls (11.4% vs 0%;  $P < 0.04$ , 11.5% vs 0%;  $P < 0.05$  respectively). CMV and EBV were not detected in non inflamed mucosa of IBD patients and EBV was detected in inflamed mucosa of one patient (16.7%) with other inflammatory conditions of the colon. When compared with inflamed mucosa of IBD patients, the differences were not statistically significant.

**Conclusion:** CMV and/or EBV have a predilection for inflamed mucosa in IBD patients. Whether the presence of CMV and/or EBV in inflamed mucosa predispose IBD patients to the development of severe steroid refractory disease remains to be determined.

## 1009

### Cost of Treating Crohn's Disease

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**Purpose:** To estimate differences in health care costs between Crohn's disease (CD) patients (pts) and controls and to examine differences in CD costs by prescription therapy.

**Methods:** Administrative claims data from geographically diverse private US health plans with service dates between Jan 1, 2002 and Dec 31, 2005 were utilized. CD pts (ICD-9-CM code 555.x) were identified and matched



to controls in a 1:5 ratio on age, gender, health plan, and duration of enrollment. Members with at least 1-year of continuous enrollment after a CD diagnosis were included; total costs (2005 US\$) were calculated by summing the amount paid by the health plan for medical services and pharmaceuticals. CD pts were grouped by drug regimen as follows: steroids, immunosuppressants (IMMS), infliximab, any combination of the 3 drug classes, and no CD-treatment or treatment not including studied regimens. Average medical and pharmaceutical cost per pt per day was estimated in each group and projected annually.

**Results:** 9,302 CD pts and 46,510 matched controls were identified. Total annual cost per pt was nearly 4 times higher in the CD group (\$11,454) than the control group (\$3,028,  $P < 0.01$ ). Costs for medical services accounted for greater than 80% of total costs in each group, \$9,762 and \$2,494, respectively. CD pts not receiving any of the studied therapies had considerably lower costs for medical services and pharmaceuticals compared to the study groups (Table). Costs of medical services among CD pts receiving a steroid in combination with another therapy were substantially higher compared to both monotherapy and combination therapies excluding steroids.

**Conclusion:** CD pts incur significantly greater costs than a similar general population. CD pts on no treatment or not receiving studied regimens incur fewer costs suggesting that they may be experiencing remission or mild symptoms. The use of steroids is associated with significantly higher medical costs, which may be suggestive of uncontrolled symptoms or flares requiring medical resources.

Mean Per Patient Per Day and Annual Costs by Drug Regimen

Groups	Medical Cost (per pt per day)	Pharmacy Cost (per pt per day)	Total Cost (annual)
No Treatment or Treatment not including Studied Regimens	14.99	4.32	6,951
Steroids	43.46	10.47	19,413
IMMS	19.96	8.95	10,407
IMMS + Steroids	50.25	13.97	23,122
Infliximab	32.74	53.01	30,871
Infliximab + Steroids	89.80	83.69	62,458
IMMS + infliximab	33.01	53.24	31,050
IMMS + infliximab + Steroids	78.17	61.34	50,224

## 1010

### Immunization for Vaccine-Preventable Illnesses in Patients with Inflammatory Bowel Disease

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**Purpose:** Vaccines are underutilized in immunocompromised patients including those with Inflammatory bowel disease (IBD) on immunosuppressive therapy, despite published guideline recommendations. IBD patients on immunosuppressive therapy are at higher risk for infections. A recent study suggests that immunization against vaccine-preventable illnesses is uncommon in IBD patients and efforts are needed to improve vaccine administration. Aim of our study was to determine the rate of immunization among patients with Inflammatory bowel disease (IBD) on immunosuppressive therapies, identify patients at risk for infection, and review reasons for non-immunization. This study was undertaken to improve performance at our institution.

**Methods:** Electronic medical records of all outpatients with IBD seen at Ochsner Clinic Foundation between September 2005 and August 2006 were

retrieved based on ICD-9 codes between September 2005 to August 2006. Patients on immunosuppressive therapy were administered a 25-point phone survey questionnaire encompassing basic medical history, IBD related medication exposure, vaccination history, previous infections with vaccine preventable diseases. Electronic medical records were assessed for hepatitis B serology and varicella titers (IgG; ELISA). Information was collected on exposure to known risk factors for acquiring selected vaccine preventable diseases.

**Results:** 798 patients were coded as having IBD during the study period. A phone survey questionnaire was administered to 189 patients on immunosuppressive therapies. Our final study population included 118 patients after excluding 71. 95 (81%) patients recalled tetanus immunization within the past 10 yrs, 53 (45%) reported annual flu shots, and 32 (27%) reported pneumococcal vaccination. One of the more common reasons for nonimmunization for influenza included lack of awareness (31%). 47 patients (40%) were at risk for HBV but only 28 (24%) were vaccinated. 27 patients could not recall a history of chicken pox; of these, 13 reported varicella immunization.

**Conclusion:** Immunization against vaccine-preventable illnesses is underutilized in IBD patients on immunosuppressive therapies. Efforts are necessary to improve immunization efforts in this at risk population.

## 1011

### Risk Factors for Pouchitis after Ileal Pouch-Anal Anastomosis for Ulcerative Colitis or Indeterminate Colitis: A Population-Based Study

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**Purpose:** Pouchitis is the most common form of pouch dysfunction following ileal pouch-anal anastomosis (IPAA). We describe a population based study of age at diagnosis, gender, PSC, and operative technique as risk factors for the development of pouchitis after IPAA.

**Methods:** The Rochester Epidemiology Project, a medical records linkage system providing data on all health care for the population of Olmsted County was used to identify all county residents with a diagnosis of UC or IC from 1940–2005 who had an IPAA. Medical records were reviewed to characterize clinical course following IPAA. The cumulative probability of developing pouchitis was estimated using the Kaplan Meier method. Gender, age at diagnosis < 30 years, PSC, and presence of a rectal cuff were assessed for association with risk of pouchitis using Cox proportional hazards regression.

**Results:** Forty-five pts were identified, all of whom had a J-shape IPAA. Six pts (13%) had their diagnosis changed to Crohn's disease (CD). Of the remaining 39 patients without CD, the median age at diagnosis of UC was 30 years. Twenty-five patients were male. Seven had PSC; 19 had a stapled anastomosis with a rectal cuff. The cumulative probability of pouchitis at 1, 5 and 10 yrs was 27%, 58% and 68%, respectively. In a multiple variable Cox model, male gender (hazard ratio [HR] 4.1, 95% CI 1.5–11.0), age at diagnosis <30 yrs (HR 3.9, 95% CI 1.5–10.0) and PSC (HR 3.2, 95% CI 1.2–8.6) were independently associated with the risk of pouchitis. The presence of a rectal cuff was not a significant risk factor. No significant two way interactions were detected.

**Conclusion:** A diagnosis of PSC, male gender and age at UC diagnosis less than 30 years were independent risk factors for the development of pouchitis after J-IPAA for UC in this population-based cohort. Previous studies have found PSC to be a risk factor for pouchitis. Young age at UC diagnosis and male gender are novel findings that could help to predict the clinical course of a patient after J-IPAA for UC.

1012

**Treatment of Inflammatory Bowel Disease with 6-Thioguanine (6-TG): Retrospective Case Series from a Tertiary Care Center**

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**Purpose:** 6-TG has been suggested as an alternative treatment option for patients with inflammatory bowel disease (IBD). However, hepatotoxicity, especially nodular regenerative hyperplasia (NRH) has been described leading to recommendation not to consider the drug for long term treatment of IBD. We would like to report our experience from a single tertiary referral center with the use of 6-TG for treatment of IBD.

**Methods:** Retrospective case series study. We reviewed patient charts including hospital and outpatient electronic record/chart of all patients followed in our adult IBD clinic over past 5 years. We identified patients on 6-TG and reviewed their charts for duration of treatment with 6-TG and adverse reactions, specifically abnormal liver function tests (LFTs), NRH and lymphoma during their follow-up.

**Results:** We reviewed the medical records of 289 patients followed in our adult IBD clinic over the past 5 years. Of these, 24 patients were treated with 6-TG, 7 male (29%) and 17 (71%) female patients, mean age of 48 years (range 17 to 86 years), 23 patients had Crohn's disease and one had ulcerative colitis. The mean duration of treatment with 6-TG was 21 months (range from 2 months to 72 months). Only 2 patients, 1 male and 1 female, had significant elevation in their LFTs on 6-TG. Both underwent liver biopsy with only one (4%) reported to have NRH on liver biopsy. This patient discontinued 6-TG, with complete normalization of his LFTs. No lymphoma was detected in any patients receiving 6-TG.

**Conclusion:** 6-TG is rarely associated with NRH. This drug has been used at our center for treatment of patients who cannot tolerate on other immunosuppressive agents. 6-TG is an alternative immunosuppressive agent that can be safely considered in the treatment of IBD. Prospective studies will be needed to further evaluate for long term safety and efficacy of 6-TG in treatment of IBD.

1013

**Characteristics of an Inflammatory Bowel Disease Population with Dysplasia and Adenocarcinoma**

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**Purpose:** Inflammatory bowel disease (IBD) is associated with an increased risk of intestinal dysplasia and neoplasia. The purpose of our study was to identify characteristics of IBD patients diagnosed with such findings.

**Methods:** Patients found to have both IBD and dysplasia or neoplasia on histology between 1994 and 2004 were identified from a pathology database of the largest healthcare system in Rhode Island and from community recruitment. A retrospective chart review was then performed to identify the demographic, historical, clinical, and histologic characteristics of qualifying patients.

**Results:** 32 IBD patients were identified as having dysplasia and/or neoplasia on histology. 25 (78%) were men, and 7 (22%) were women. Of the patients for whom information was available, 24 (83%) had ulcerative colitis (UC) and 5 (17%) had Crohn's disease (CD). 21 of 32 patients (66%) had low or moderate grade dysplasia, 5 of 32 (16%) had high grade dysplasia, and 13 of 32 (41%) had adenocarcinoma, with 8 of 32 patients (25%) having more than one of the above findings concurrently. 5 of 20 IBD patients (25%) had their dysplasia or neoplasia found during IBD surveillance while the other 15 (75%) were diagnosed either incidentally or due disease symptoms. The average age of the 13 patients with neoplasia was  $60 \pm 17$  years while it was  $56 \pm 17$  years for the 13 patients without neoplasia. Of 13 patients with UC, 11 (85%) had pancolitis and 2 (15%) had solitary left-sided disease. Only

2 of 17 patients (12%) had a family history of colon cancer and no patients had a history of primary sclerosing cholangitis.

**Conclusion:** A population of IBD patients from a large healthcare system in Rhode Island found to have dysplasia or neoplasia was predominantly male and without family history of colorectal cancer. Most had ulcerative colitis with pancolitic involvement and none had primary sclerosing cholangitis. The majority had their diagnoses made incidentally or because of disease symptoms, not during IBD surveillance. The most common diagnoses were low or moderate grade dysplasia or neoplasia. The average age of the subgroup of patients with neoplasia was similar to those patients with dysplasia without neoplasia.

1014

**Safety and Efficacy of Adalimumab in Pediatric Crohn's Disease Patients**

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**Purpose:** Attenuated response or anaphylaxis may develop to infliximab. Adalimumab has recently emerged in the adult Crohn's Disease (CD) population as an alternate TNF-alpha inhibitor. No studies of adalimumab use in pediatric pts with CD have been reported. Our study aim was to examine the safety and efficacy of adalimumab in pediatric CD pts.

**Methods:** Records of 15 pediatric pts with CD who received adalimumab (Humira®, Abbott Laboratories, Abbott Park, IL) were reviewed per an IRB approved protocol. All pts had a prior attenuated response or anaphylaxis to infliximab. Pts and/or caregivers were trained on SQ administration of adalimumab at home. They were to call the physician's office if they experienced any illness or adverse reaction between visits. Other medications remained the same. Clinical response to adalimumab was classified as complete response, partial response, or nonresponse.

**Results:** 15 pts with CD were prescribed adalimumab over a 33 month period. One pt was lost to follow-up. 14 had adequate follow-up for review. Average age at start of therapy was 16.6 (10.3–21.8) yrs. M:F ratio was 3:4. The majority of pts received an 80 mg loading dose and 40 mg q2 wks. Average duration of therapy was 10.8 months. A total of 272 injections were given. Of the 14 pts, 7 (50%) had complete response, 2 (14%) had a partial response, and 5 (36%) had no response to adalimumab. Complete response was achieved on average after 5 injections. Of 5 pts with fistulizing disease, 3 maintained fistula closure; 1 had temporary closure and 1 pt required surgery. 26 adverse events occurred during 272 doses (9.6%). The most common adverse events were abdominal pain and nausea. There were no serious adverse events and no adverse events required adalimumab discontinuation. Therapy was discontinued in 2 pts due to insurance denial.

**Conclusion:** Adalimumab was well tolerated in our pediatric pts with CD, with 67% responding favorably. No serious adverse events occurred. Further studies are needed to evaluate efficacy and determine optimal dosing of adalimumab in this population.

1015

**Family Medicine Practitioners Often Uncomfortable Providing Preventive Care to Inflammatory Bowel Disease Patients**

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**Purpose:** Inflammatory bowel disease (IBD) patients may not receive preventive care at the same rate as the general population. Attitudes of primary care providers may be a key factor.

**Methods:** We conducted an anonymous, cross-sectional survey of family medicine practitioners. The survey consisted of 9 demographic items, 2

items to assess comfort level with IBD patients and 6 vignettes of preventive care issues.

Multiple choice answers were designated to represent a range of attitudes toward primary care in IBD patients: 1) active response to perform appropriate preventive health action; 2) minimal involvement; 3) generic lack of involvement and 4) complete lack of involvement based on concept of severe disease state.

**Results:** 42 of 97 surveys were returned. 7/924 responses were left blank (0.75%).

Degrees of subjects were as follows: MD 83%, physician assistant 12%, doctor of osteopathy 2% and international medical graduate 2%. Mean year of graduation was 1986. Mean age of subjects was 48. Women comprised 31% of the group. 90% of subjects practice family medicine. 88% of subjects practice mainly in outpatient settings. 16% indicated they were not comfortable with primary care for any patients currently using medical therapy for IBD. But 40% of subjects felt comfortable providing primary care across a range of illness severity, which compares with 48% who reported moderate/high exposure to IBD patients.

Vignettes 1 and 6 concerned reaction to mild hypertension. 90% of subjects' answers represented an attitude of active involvement.

Vignette 2 elicited attitudes to lipid measurement in IBD patients. 63% endorsed active response.

Vignette 3 assessed attitudes toward cardiovascular risk reduction. 87% endorsed an active role.

Vignette 4 addressed need for vaccines in a young patient on maintenance infliximab. Only 26% answered that they would take an active role to vaccinate this person.

Vignette 5 also involved vaccines but the age of the patient was 65. 70% of subjects chose the active role.

No subject endorsed complete lack of involvement based on a concept of severe disease state.

**Conclusion:** Our study suggests family medicine doctors are uncomfortable caring for IBD patients. Unfamiliarity with medications may be key and explain low endorsement of vaccines for a case patient on infliximab.

## 1016

### An Audit of Tolerability and Adverse Effects of Azathioprine and 6-Mercaptopurine in Patients with IBD

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**Purpose:** To determine: 1) the percentage of patients who stopped azathioprine or 6-MP due to adverse reactions, 2) The side effect profile of these treatments.

**Methods:** The case records of the patients with IBD, on immunosuppressive treatment from 2001 to 2007 under gastroenterology follow up were examined, in a district hospital in the north of England, looking after a population of 200,000.

**Results:** A total of 56 patients were identified who received treatment with azathioprine. In 32 patients (57%), (average age 36.3) medication had to be stopped due to side effects, after an average follow up of 233 days, (median 94 days). The medication was stopped due to abdominal or chest pain in 16, (50%). The other side effects were as follows: Nausea or vomiting, 10 patients (31%), hepatitis or abnormal liver function tests (LFTs), 7 (22%), dizziness 2 (6%), headache 2, (6%), pancreatitis 1 (3%), leucopenia or neutropenia in 3 patients, (9%) (One was restarted after 2 weeks in a lower dose).

Out of these patients 9 patients were given 6 MP, 3 of them did not tolerate this medication either, but 6 were able to tolerate it without significant side effects. 6 patients were initiated on 6 MP, without previously having received azathioprine and they were all able to continue it, (100%).

**Conclusion:** In our cohort of patients, a majority had to stop azathioprine due to side effects, the commonest of which was abdominal pain, nausea or vomiting and abnormal LFTs. 6-MP seems to be better tolerated, and should be considered as a first line treatment.

## 1017

### ABSTRACT WITHDRAWN

## 1018

### The Safety of Natalizumab in Patients with Relapsing Multiple Sclerosis: An Update from TOUCH and TYGRIS

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**Purpose:** To report an update on the safety of natalizumab in relapsing multiple sclerosis (MS) patients.

**Methods:** The TOUCH Prescribing Program is an ongoing, mandatory safety registry in the US designed to ensure appropriate and informed use of natalizumab; determine the incidence of and risk factors for serious opportunistic infections (OIs), including PML; and monitor patients for signs and symptoms of PML. Physicians report on PML and serious OIs, deaths, and natalizumab discontinuations. TYGRIS is a global observational study with an expected enrollment of approximately 5000 patients. It was designed to investigate the long-term safety of natalizumab in a clinical practice setting. Patients in TYGRIS are evaluated at baseline and every 6 months thereafter for 5 years, regardless of natalizumab treatment status. Data collected at each evaluation include medical/MS history; prior natalizumab use; prior use of immunomodulatory, antineoplastic, or immunosuppressive agents; and all serious adverse events, including PML, serious OIs, and malignancies.

**Results:** As of February 23, 2007, 5716 patients have been enrolled in TOUCH and 114 patients have been enrolled in TYGRIS. The most current exposure and safety data from patients receiving natalizumab worldwide will be presented.

**Conclusion:** Updated safety results from TOUCH and TYGRIS will continue to expand our knowledge on the long-term safety of natalizumab in relapsing MS.

## 1019

### Item Content Validation for Two New Measures To Assess Crohn's Disease Patients' Interest in Medication Change

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**Purpose:** To develop content for two new clinical aids; a brief Screening Tool that identifies Crohn's disease (CD) patients' with an interest in medication change and a Monitoring Tool that provides a detailed assessment of patients' treatment experiences.

**Methods:** Two internet focus group sessions were conducted with patients (N = 34) from a US CD panel managed by MRxHealth. Participants in each session were balanced by age, gender, self-rated symptom severity (remission, mild, moderate and severe), and desire to switch medication (1/3 recent switch, 1/3 want to switch, 1/3 see no need to switch). A conceptual model of CD's impact on health-related quality of life provided the basis for a qualitative inquiry of: (1) troublesome physical and psychological CD symptoms, (2) optimal and troublesome medication attributes, and (3) CD's impact on patient's life. Respondent transcripts were thematically coded and the most frequently mentioned themes identified measurement domains and allowed for the design of general and specific items for each domain. Participants later responded to these items about the impact of CD and its treatments over the last two weeks. Logistic regression analysis was used to select the best predictors of participant interest in medication change.

**Results:** Six domains were identified and a general Screening Tool item designed for each (GI symptom control, treatment side effects, emotional distress, impact on significant relationships, social and community function, and work/school/home productivity). Ratings of specific items in each of the 6 domains accounted for 14%-77% of the variance in participants' interest in medication change. Three items in each domain that most correlated with interest in medication change were included in the Monitoring Tool.

**Conclusion:** Results from this initial study indicate that items predicting patients' interest in medication change involves symptomatic factors, as well as the impact of uncontrolled symptoms and treatment side effects on patients' lives. The Screening and Monitoring tools will be subsequently tested in a larger CD patient population to validate their use in clinical settings.

## 1020

### Gastroenterologists' Tolerance for Crohn's Disease Treatment Risks

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**Purpose:** To quantify gastroenterologists' maximum acceptable risk (MAR) for treatment-related serious adverse events (SAEs) in Crohn's disease (CD) patients.

**Methods:** Gastroenterologists completed a series of choice-format conjoint trade-off tasks, choosing 1 of 2 treatments for each of 3 patients (young, middle-aged, and elderly with randomly assigned gender and number of prior surgeries). Treatment attributes included daily symptom severity and activity limitations, potential for CD complications, time between flare-ups, oral steroid use, and varying levels of three SAE mortality risks: serious infec-

tion, progressive multifocal leukoencephalopathy and lymphoma. Random-parameters logit was used to obtain relative trade-off weights and calculate the annual SAE-specific MAR for various benefit levels.

**Results:** A total of 315 gastroenterologists provided usable data for analysis. Their mean (SD) age and years in practice were 48 (9) and 15 (3) years, respectively. They treated a mean (SD) of 29 (31) CD patients in a typical month. Improvement in daily symptom severity was the most important factor in treatment selection. Greater risk acceptance was seen for treatments with higher levels of clinical benefit. In comparison to their preferences for middle-aged patients, they were less tolerant of SAE risk for young patients and more tolerant of risk for elderly patients. Risk tolerance was greatest for the lymphoma SAE across all age groups, but particularly for elderly patients. For improvements from severe CD to mild CD or remission, patients' preferences obtained from a parallel study are similar to that of gastroenterologists when they are prescribing for middle-aged patients. However, patient respondents were generally twice as willing to accept SAE-related risk for improvements from moderate CD symptoms.

**Conclusion:** Medical interventions carry risks of adverse outcomes that must be evaluated relative to their clinical benefits. Gastroenterologists are willing to accept defined mortality risks in exchange for clinical efficacy and their acceptance is affected by the degree of benefit offered by the treatment, the patient's characteristics and the nature of the SAE. Compared to prescribing physicians, patients are more willing to accept risk to avoid moderate CD symptoms.

## 1021

### Assessment of the Validity of Computed Tomographic Enterography for Diagnosing Active Crohn's Disease

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**Purpose:** Emerging research suggests that computed tomographic enterography (CTE) provides a noninvasive method for diagnosing Crohn's disease (CD). Many CTE studies have shown a correlation between CTE and standard diagnostic techniques for assessing CD of the small bowel. This retrospective review evaluated the validity of CTE for assessing CD in patients with anal, rectal, colonic, and small bowel involvement with or without fistulous disease.

**Methods:** Medical records for consecutive adult patients with suspected or confirmed CD who had undergone CTE for active disease assessment or routine evaluation were reviewed. Results from CTE were compared with those from other diagnostic and interventional assessments, including colonoscopy, capsule endoscopy (CE), and direct surgical examination.

**Results:** The analysis included 25 patients (mean age, 41 y); 18 had previous CD diagnosis, and 7 had no prior CD history. Of the patients with diagnosed CD, 5 had CD involving the small bowel only, 3 had colonic, anal, and/or rectal involvement only, and 10 had CD involving multiple locations; 7 had prior bowel resection, and 6 had current fistulas. Additional assessments were conducted within 14 months of CTE (median, 3 wk; range, 2 d-14 mo). Patients underwent colonoscopy only (N = 15), colonoscopy with CE (N = 5), CE only (N = 1), or surgical intervention (N = 4). Results of CTE were in concordance with 74% of colonoscopy and CE results. Concordance was observed between CTE and colonoscopy for diagnosing ileal or colonic/rectal disease activity (N = 5 and N = 6, respectively) and lack of ileal or colonic/rectal disease activity (N = 3 and N = 4, respectively) and between CTE and CE for ileal disease activity (N = 1) and lack of small bowel disease activity (N = 1). Concordance between CTE and surgical examination or colonoscopy for detecting fistulae was 50%, with CTE detecting perianal (N = 1) and enteroenteric (N = 2) fistulae.

**Conclusion:** In this retrospective study, CTE demonstrated a high level of agreement with standard diagnostic measures and direct surgical evaluation on assessments of active ileal or colonic CD. These findings suggest CTE may provide a valuable, noninvasive diagnostic tool with detection capabilities complementary to more invasive techniques. The fact that CTE demonstrated a moderate capability for diagnosing active fistulous disease suggests a potential need for more sensitive techniques for detecting fistulae.

1022

### Natalizumab Induces Sustained Response and Remission in the Absence of Concomitant Immunosuppressants in Patients with Crohn's Disease Who Failed Prior Anti-TNF $\alpha$ Therapy

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**Purpose:** This post-hoc analysis assessed the need for concomitant immunosuppressants (IMM) for induction and maintenance of response and remission with natalizumab (NAT) in patients (pts) who failed prior anti-tumor necrosis factor  $\alpha$  (TNF $\alpha$ ) therapy.

Table 1

Month	Response		Remission	
	PBO	NAT	PBO	NAT
1	33	43	10	13
2	22	50*	8	19
3	28	54*	10	22*
2 & 3	14	41*	4	15*

\* $P < 0.05$ 

Table 2

Month	Response		Remission	
	PBO	NAT	PBO	NAT
6	21	48	11	43*
9	11	43*	11	43*
12	11	43*	11	43*

\* $P < 0.05$ 

**Methods:** In the ENCORE induction trial, 509 pts with CDAI scores  $\geq 220$  and  $\leq 450$  and CRP levels  $> 2.87$  mg/L were randomized 1:1 to receive NAT (N = 259) or placebo (PBO; N = 250) at Mths 0, 1 and 2. In the ENACT2 maintenance trial, NAT-treated pts who had responded in ENACT1 and had

a CDAI score  $< 220$  were re-randomized 1:1 to receive monthly NAT (N = 168) or PBO (N = 171) for up to 12 mths.

**Results:** In ENCORE, 54 NAT- and 51 PBO-treated pts failed prior anti-TNF $\alpha$  therapy and did not receive IMM at baseline. Within this subgroup a significantly greater proportion of NAT-treated pts were in clinical response at Mths 2 and 3 and at both timepoints combined, compared to PBO (Table 1). A significantly greater proportion of NAT-treated pts were in clinical remission at Mth 3 and sustained remission through Mths 2 and 3 compared to PBO (Table 1). In ENACT2 21 NAT- and 19 PBO-treated pts failed prior anti-TNF $\alpha$  therapy and did not receive IMM at baseline. NAT treatment resulted in more pts in clinical response and remission throughout the study compared to PBO (Table 2). Significant differences in response and remission were observed, respectively, at Mths 9 through 12 and at Mths 6 through 12 (Table 2).

**Conclusion:** Analyses of these trials suggest that NAT was effective in inducing response and maintaining remission in CD pts who failed prior anti-TNF $\alpha$  therapy and did not receive concomitant IMM.

1023

### Adverse Events Related to the Use of Corticosteroids, Immunosuppressants, and Anti-TNF $\alpha$ Therapy in Crohn's Disease Patients

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**Purpose:** To assess adverse event (AE) rates associated with anti-tumor necrosis factor  $\alpha$  (TNF $\alpha$ ) therapy, steroids, and steroid/TNF $\alpha$  combination (S/TNF $\alpha$ ) used in the treatment of Crohn's disease (CD) patients (pts).

**Methods:** De-identified medical and pharmacy claims data with service dates between Jan 1, 2002 and Dec 31, 2005 from geographically diverse private US health plans were used for the analysis. CD pts were identified using ICD-9-CM diagnosis code 555.x. At the time of an AE, pts were grouped by therapy regimen: steroids, TNF $\alpha$ , S/TNF $\alpha$ , or referent group (immunosuppressants, 5-aminosalicylates, and antibiotics). A Cox proportional hazards model was used to estimate AE hazard ratios (HRs) in person time units with Wald tests to assess statistical significance between groups.

**Results:** 8,581 CD cases were identified. Compared to the referent group, steroids, TNF $\alpha$ , and S/TNF $\alpha$  were generally associated with increased risk of sepsis, demyelinating conditions, opportunistic infections, and encephalopathy or encephalitis (Table). For demyelination and sepsis, the risk for S/TNF $\alpha$  therapy was elevated compared to steroids alone, while for all acute AEs, the risk from S/TNF $\alpha$  therapy was elevated compared to TNF $\alpha$  alone. Analyses with immunosuppressants as a separate regimen group did not influence the outcome of examined events; they were combined into the referent treatment group.

**Conclusion:** Commonly used therapies for CD have been associated with an increased risk of AEs. These results show excess risks for certain AEs in pts using steroids or TNF $\alpha$  with increased risk for S/TNF $\alpha$  combination use.

Table. Hazard ratios for selected AEs by regimen groups

	Steroids only 541 pt-yrs	anti-TNF $\alpha$ only 434 pt-years	S/ anti-TNF $\alpha$ combination 49 pt-years
AEs	Hazard ratio vs referent group		
Sepsis (N = 2,113)	1.49*	1.55*	2.66*†
Demyelination/multiple sclerosis/ optic neuritis (N = 39)	5.48*	1.33	25.21*†
Opportunistic infections (N = 379)	3.68*	1.57	4.41*
Encephalopathy, encephalitis, meningitis (N = 593)	2.65*	1.10	4.82*
Any acute event (N = 3,365)	1.83*	1.40*	2.71*††
Any adverse event (N = 7,352)	1.45*	1.21*	1.70*

\*95% CI does not include 1.0; † $P < 0.10$  for combination therapy vs steroids alone; †† $P < 0.10$  for combination therapy vs TNF $\alpha$  alone

Further research should assess the benefit and risk of using these therapies independently or in combination for the management of CD patients.

## 1024

### Lactoferrin Assessment of Rectal Effluent as an Aid to Colonoscopy for Determining Intestinal Inflammation

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**Purpose:** Accurate evaluation of intestinal inflammation is vital in the management of inflammatory bowel disease (IBD) patients. A limitation of conventional colonoscopy is the inability to visualize the entire intestinal tract. Fecal lactoferrin, a marker of intestinal inflammation, may function as an aid to colonoscopy for assessing IBD patients. Our aim was to evaluate lactoferrin levels in rectal effluent in conjunction with colonoscopy to assess the presence of inflammation in IBD patients undergoing screening or diagnostic colonoscopy.

**Methods:** Fifty-nine adult IBD patients from a single tertiary care center were enrolled. Each subject provided a sample of the effluent passed towards the end of the bowel preparation procedure prior to colonoscopy. The specimens were screened for elevated lactoferrin using the IBD-CHEK®, a commercially available enzyme-linked immunosorbent assay (ELISA) (TechLab, Blacksburg). There were 27 active patients and 32 inactive patients based on colonoscopy and histology.

**Results:** Forty-four Crohn's disease (CD) and 15 ulcerative colitis patients were included in the study. The median age was 44 (22–72) and there were 42 females and 17 males. The lactoferrin ELISA had 74.1% sensitivity, 84.4% specificity, and 79.7% correlation with colonoscopic findings. Five patients characterized as inactive by colonoscopy had moderately high lactoferrin levels. Four of these patients had Crohn's disease, and the elevated lactoferrin may represent inflammation unseen by conventional colonoscopy. This suggests a role for lactoferrin testing to help target CD patients requiring additional testing such as small bowel radiography. Seven samples with endoscopically defined inflammation were negative on the lactoferrin ELISA.

**Conclusion:** Rectal effluent samples are easily obtained with a relatively high degree of patient compliance. Testing for lactoferrin provides an aid to colonoscopy for determining intestinal inflammation. A positive lactoferrin result in an endoscopically inactive patient may indicate unresolved inflammation but further investigation is needed. A negative result in an effluent sample is not clinically relevant due to the potential dilution of lactoferrin during the bowel preparation procedure and should not be used to rule out the presence of intestinal inflammation.

## 1025

### Natalizumab Does Not Require the Concomitant Use of Immunosuppressants or Corticosteroids for the Induction of Sustained Response and Remission in Patients with Crohn's Disease

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University, Budapest, Hungary; University of Amsterdam Medical School, Amsterdam, Netherlands; Hepato-Gastroenterology, Hradec Králové, Czech Republic and Cedars Sinai, Los Angeles.

**Purpose:** This post-hoc analysis assessed the need for concomitant immunosuppressants (IMM) or corticosteroids (CS) for induction of response and remission with natalizumab (NAT) in the ENCORE and ENACT2 trials.

**Methods:** In the ENCORE induction trial, 509 patients (pts) with CDAI scores  $\geq 220$  and  $\leq 450$  and CRP levels  $> 2.87$  mg/L were randomized 1:1 to receive NAT 300 mg (N = 259) or placebo (PBO; N = 250) infusions at Mths 0, 1, and 2. In the ENACT2 maintenance trial, NAT-treated pts who responded in ENACT1 and had a CDAI score  $< 220$  were re-randomized 1:1 to receive monthly NAT (300 mg; N = 168) or placebo (N = 171) infusions for up to 12 mths.

**Results:** In ENCORE, 188 pts were not receiving IMM or CS at baseline, with 90 and 98 randomized to receive NAT and PBO, respectively. A significantly greater proportion of NAT-treated pts were in clinical response at both Months 2 and 3, and, individually, at Mths 1 through 3, compared to the PBO group (Table 1). NAT treatment also resulted in a significantly greater proportion of pts in clinical remission at both Mths 2 and 3 and, individually, at Mths 1 and 3 compared to PBO (Table 1). In ENACT2, 138 pts were not receiving IMM or CS at baseline, and following randomization, 70 and 68 pts received NAT and PBO, respectively. At Mths 6 through 12, a significantly greater proportion of NAT-treated patients were in clinical response and remission, compared to the PBO group (Table 2).

**Conclusion:** Analyses of these trials suggest that NAT was effective in inducing response and sustaining remission in CD pts in the absence of concomitant IMM or CS therapy.

**Table 1.** ENCORE (Induction)

Month	Response		Remission	
1	36	54*	8	22*
2	40	56*	19	28
3	40	62*	22	39*
2 and 3	31	51*	12	24*

\*P < 0.05

**Table 2.** ENACT2 (Maintenance)

Month	Response		Remission	
6	38	67*	34	56*
9	35	64*	31	51*
12	24	59*	22	54*

\*P < 0.05

## 1026

### Do Patients with Inflammatory Bowel Disease Worry about Their Risk of Colon Cancer? A Study of Patients' Perception of Their Own Colon Cancer Risk

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**Purpose:** Patients with chronic, extensive ulcerative or Crohn's colitis have an increased risk of colon cancer (about 0.5–1% per year after 8–10 years of disease) and need colonoscopic surveillance every 2 years. The purpose of this study is to assess patients' perceptions of their own risk of colon cancer and to see if this relates to adherence to surveillance colonoscopy.

**Methods:** 259 patients with UC or Crohn's colitis for at least 7 yrs and at least 1/3 of the colon involved participated in this cross-sectional questionnaire study. A chart review was also performed for each patient.

**Results:** Median age was 48, and median disease duration 20 yrs. 44% of patients had UC, and 51% were female. 49% of patients had waited more than 2.5 yrs between exams and 40% of patients had waited longer than 3 yrs between exams. The mean perceived risk of developing colon cancer during each patient's lifetime without having routine colonoscopies was 53%. In comparison, the mean perceived risk of developing colon cancer *with* routine colonoscopies was 36%. On a 0–10 scale, with 0 being no worries and 10 being extremely worried, the average worry of IBD patients for developing colon cancer was 5.09. When asked to consider their level of worry of getting colon cancer compared to the average person without IBD, IBD patients had a mean of 3.39 times more worry. When asked how much risk (number of times more likely for developing colon cancer compared to someone without IBD) would cause them to never miss a colonoscopy, IBD patients responded that they would have to be on average 11.97 times more likely to get colon cancer in order to have a colonoscopy. Adherence was not related to worry level or perceived risk.

**Conclusion:** IBD patients perceive that routine surveillance colonoscopies reduce their risk of colon cancer development by about 17%. However, our IBD patients would accept a mean of an almost 12-fold increased risk of colon cancer, compared to an average person without IBD, before they would adhere to surveillance colonoscopy. In addition, our IBD patients report a more than three-fold increased worry level about developing colon cancer compared to an average person without IBD. Worry level or perceived risk, however, did not relate at all to adherence.

## 1027

### Chronic Perceived Psychological Stress and the Regulation of Pro-Inflammatory Cytokines in Ulcerative Colitis

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**Purpose:** While the etiology of IBD remains unclear, alterations in cytokine profiles are key pathophysiological determinants. Psychological stress has been associated with a diverse array of adverse health outcomes and there is compelling evidence it can modulate the clinical course and severity of IBD. Data from experimental models suggest that the effects of stress on intestinal inflammation are mediated through various neuroendocrine-immune signaling pathways. The hypothalamic pituitary adrenal (HPA) axis is activated during the stress response and plays a central role in the regulation of immune function during this period. Thus, the goal of the present study was to determine the effects of the synthetic glucocorticosteroid receptor agonist, dexamethasone (DEX) on LPS-stimulated pro-inflammatory cytokine production by PBMC from ulcerative colitis (UC) patients in remission compared to healthy control subjects.

**Methods:** 20 patients with established UC in clinical remission for at least 3 months were recruited from the IBD clinic. None of the patients were receiving oral or topical steroids as maintenance therapy. Age and gender matched healthy subjects were recruited as controls. Glucocorticosteroid sensitivity of LPS induced TNF  $\alpha$ , IL 6 and IL 1 $\beta$  production in whole blood samples was measured using DEX at a final concentration of 0 nM (basal), 10 nM, 50 nM and 100 nM. Levels of chronic (1 month) perceived psychological stress were measured using the 10 item Perceived Stress Scale (PSS).

**Results:** Patients with UC exhibited significantly less suppression of TNF $\alpha$  production expressed as a proportion of the level measured in the absence of DEX (.91  $\pm$  0.05 vs. .53  $\pm$  0.06 10 nM; .54  $\pm$  0.06 vs. .28  $\pm$  0.07 50 nM; .37  $\pm$  0.06 vs. .19  $\pm$  0.05 100 nM.  $P < 0.01$  in each instance). Significantly less inhibition of IL 6 (.89  $\pm$  0.04 vs. .65  $\pm$  0.05 10 nM; .65  $\pm$  0.06 vs. .29  $\pm$  0.05 50 nM; .43  $\pm$  0.05 vs. .20  $\pm$  0.06 100 nM) and IL 1 $\beta$  (.84  $\pm$  0.07 vs. .56  $\pm$  0.05 10 nM; .52  $\pm$  0.07 vs. .23  $\pm$  0.05 50 nM; .31  $\pm$  0.05 vs. .12  $\pm$  0.04 100 nM) production were also observed ( $P < 0.01$  in each instance). Finally, higher levels of chronic perceived stress were observed in UC patients compared to healthy controls (21.6  $\pm$  4.3 vs. 12.4  $\pm$  3.2;  $P < 0.01$ ).

**Conclusion:** These observations suggest that glucocorticoid resistance of pro-inflammatory cytokine synthesis may represent a novel pathway by which

chronic stress may alter the clinical course of ulcerative colitis. Potential mechanisms may include the downregulation of glucocorticosteroid receptors on immune cells.

## 1028

### Serologic Markers Are Associated with Subsequent Crohn's Disease Diagnosis and Fistulous Complications in Ulcerative Colitis Patients Who Undergo Ileal Pouch Anal Anastomosis

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**Purpose:** Approximately 5% of patients undergoing ileal pouch-anal anastomosis (IPAA) for a diagnosis of ulcerative colitis (UC) are subsequently diagnosed with Crohn's disease (CD). In this case-control study, the association of serologic markers with the development of CD after IPAA for UC was evaluated.

**Methods:** 12 cases and 25 controls were enrolled during routine office visits to Boston Medical Center. The cases were initially diagnosed with UC, underwent IPAA, and subsequently diagnosed with CD. The diagnosis of CD was made by the patients' surgeon or gastroenterologist based on clinical course and by standard criteria including inflammation of small bowel mucosa proximal to the pouch, development of pouch fistula more than 3 months after ileostomy closure, etc. The controls were UC patients who underwent IPAA and had a normal post-operative course defined as: no change in diagnosis to CD, < 2 episodes of acute pouchitis/yr, and no pouchitis within the last 6 months. Demographic and clinical factors were recorded. Serum drawn at the time of last follow up was assayed by Prometheus Laboratories for ASCA IgG and IgA, Omp C, anti-CBir1, and pANCA using ELISA.

**Results:** The mean time to diagnosis of CD for the cases was 4.5 years. Mean follow up time for the control group was 7.4 years. 7 patients developed fistulous complications. On average, the cases had higher titers of each marker with the exception of Omp-C. There was a trend of sero-positivity for ASCA-IgA in the cases that developed CD: 42% (5/12), compared to controls 12% (3/25),  $P = 0.08$ . Those that developed fistulae were associated with sero-positivity for both ASCA IgA and anti-CBir1: 43% (3/7) compared to 6% (2/30) in those that did not develop fistulae,  $P = 0.04$ . Subjects who were ASCA-IgA + were 5.24 times more likely to be diagnosed with CD. Subjects that were both ASCA IgA + and anti-CBir1 + were 10.5 times more likely to develop fistulous complications.

**Conclusion:** UC patients that underwent IPAA and had their diagnosis changed to CD were more likely to be seropositive for ASCA IgA, and those seropositive for both ASCA IgA and anti-CBir1 were more likely to have had fistulous complications. A larger study to validate these findings is ongoing.

## 1029

### Recurrent Colon Cancer or Dysplasia after Segmental Resection in Crohn's Colitis

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**Purpose:** In ulcerative colitis, total proctocolectomy is the treatment of choice for patients with colonic dysplasia or cancer because of the high risk for recurrent neoplasia. It is unknown whether patients with Crohn's colitis and cancer or dysplasia have a similar risk. The aim of this study was to determine the risk of subsequent colon cancer or dysplasia after segmental resection or subtotal colectomy for dysplasia or cancer in patients with Crohn's colitis.

**Methods:** Seventeen patients with Crohn's disease and colon cancer or dysplasia that had been removed by segmental resection or subtotal colectomy were identified in The Mount Sinai Medical Center's pathology database. Patient records and colonoscopy reports were reviewed to identify the presence or absence of subsequent colon cancer or dysplasia in these patients during follow-up.

**Results:** Follow-up data were available for 12 patients. Nine of the 12 patients had colon cancer in their original resected specimens; 8 of the 9 had a segmental resection and one had a subtotal colectomy with ileosigmoid anastomosis. The remaining 3 of the 12 patients had dysplasia; two of them underwent segmental resection and the third had a subtotal colectomy with ileosigmoid anastomosis. At the time of surgery, the average duration of disease was 23.1 years (range 5.7–43.9). The mean length of follow-up was 7.2 years (range 1.2–22.4 yrs). One patient developed colon cancer 5.9 years after his original segmental resection for colon cancer. One patient developed a metastatic lesion 2 years after her segmental resection for cancer. A third patient developed low grade dysplasia 4.6 years after a segmental resection for high grade dysplasia. There has been no evidence of metachronous dysplasia or cancer in the remaining 9 patients, in whom the mean follow-up has been 7.5 years (range 1.2–22.4).

**Conclusion:** The heightened risk of recurrent colorectal neoplasia should be reviewed with patients prior to surgery. Proceeding with segmental resection or subtotal colectomy should be accompanied by insistence upon close post-operative colonoscopic surveillance.

### 1030

#### Long-Term Results of Adalimumab Treatment in Subjects with Moderately to Severely Active Fistulizing Crohn's Disease Who Have Failed Response or Showed Intolerance to Infliximab

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**Purpose:** We evaluated the long-term efficacy and safety of adalimumab, a fully human monoclonal antibody anti-TNF, in the induction and maintenance of perianal fistula closure in subjects with fistulizing Crohn's disease (CD) who had lost response to or were intolerant of infliximab.

**Methods:** In this observational, open-label, multi-centre, prospective study, subjects were treated with subcutaneous adalimumab: 160 mg at week 0, 80 mg at week 2, then 40 mg eow for 52 weeks. Subjects were assessed for complete or partial, ( $\geq 50\%$ , decrease in number of draining fistulas) fistula closure, PDAI score, and adverse events (AE).

**Results:** In 24 subjects with fistulizing CD (CDAI  $< 220$ ; N = 10) or luminal and fistulizing CD (CDAI  $> 220$ ; N = 14), the mean duration of CD was  $8.7 \pm 6.4$  years. At baseline, 79% of subjects were on AZA/6MP and 37% were on corticosteroids, 29.2% showed loss of response and 70.8% intolerance to infliximab, the PDAI score overall was  $10.8 \pm 2.8$ , and the mean number of draining fistulas was  $3.3 \pm 3.7$ . Long-term overall results are presented in the table.

**Conclusion:** Adalimumab treatment maintains long-term reduction in PDAI levels and complete or partial perianal fistulae closure in subjects with fistulizing CD who had failed response or showed intolerance to infliximab. No new safety concerns were found compared to other adalimumab-treated populations.

### 1031

#### Adalimumab Safety in Crohn's Disease Patients: Open-Label Maintenance Following the Gain and CHARM Trials

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**Purpose:** Adalimumab (ADA) is approved for the induction and maintenance of remission in adults with moderate to severe Crohn's disease (CD) and has demonstrated efficacy and safety in patients with and without prior anti-TNF experience.[1–3]

**Methods:** We assessed the safety of ADA maintenance therapy in patients who completed either of two Phase III, double-blind, placebo-controlled, adalimumab safety and efficacy trials, GAIN (4-week induction in infliximab failures) and CHARM (1-year maintenance). Patients had active CD (CDAI 220–450) and included those naïve to prior anti-TNF therapy (approximately 50% of 854 patients in CHARM) or who had lost response to/were intolerant of prior infliximab therapy (GAIN). Safety was routinely assessed throughout the Phase III trials and the open-label extension (OLE). Adverse events (AE) were tabulated in events/100-patient-years (E/100 PY) through 1 year in the OLE (combined data, representing 1 year since the start of GAIN and 2 years since the start of CHARM).

**Results:** Of 1169 patients, all had received ADA in either GAIN (N = 315) or CHARM (N = 854) [including during the OLE]. Adverse events of interest are listed (table). Non-systemic candidiasis comprised 27 of the 28 opportunistic infection AEs, with 1 case of coccidioidomycosis. Of the 21 malignant AEs, 11 were skin cancers and 1 was a lymphoma; the remainder were widely scattered.

Events of Interest: GAIN/CHARM combined (N = 1,169; 1,299 PY)	
Adverse Event (AE)	E (E/100 PY)
Any AE	9,979 (768)
Any Serious AE	456 (35)
AE leading to discontinuation	284 (22)
Infectious AE	1,793 (138)
Serious infectious AE	82 (6)
Injection-site reactions	388 (30)
Opportunistic infection AE	28 (2.2)
Malignant neoplasms AE	21 (1.6)
Death	2 (0.2)

**Conclusion:** Adalimumab has proven to be well-tolerated in the treatment of Crohn's disease after the 1-year follow up of patients from GAIN, and the 2-year follow up of patients from CHARM. This Crohn's disease adalimumab

#### PDAI and Fistula Closure Status Over Time in Subjects Treated With Adalimumab

	Basal	Week 4	Week 12	Week 20	Week 42	Week 52
Patients (n)	24	23	20	16	12	12
PDAI	10.8	5.8	5.6	3.8	3.4	4.4
Number of draining fistulae	3.3	0.86	1.21	0.47	0.27	1.0
Complete fistula closure (%)	–	20.8	16.7	20.8	29.2	29.2
Partial fistula closure (%)	–	41.7	37.5	37.5	41.7	41.7

ITT analysis



safety profile is consistent with the profiles in the original studies, as well as with the safety profile from other adalimumab indications. 1. Sandborn WJ, et al. *Ann Intern Med.* 2007;146(12):829–838. 2. Colombel JF, et al. *Gastroenterology.* 2007;132:52–65. 3. Schiff MA, et al. *Ann Rheum Dis.* 2006;65:889–894.

## 1032

### Participation in Colonoscopic Cancer Surveillance among Patients with Ulcerative Colitis: Meeting Expectations?

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**Purpose:** To prevent colorectal cancer in ulcerative colitis (UC), major gastroenterology societies recommend an intensive program of colonoscopic screening/surveillance every 1–2 years beginning 8 years after disease onset. In patients without UC, rates of participation in colonoscopic screening programs have been well described. However in patients with UC, rates of participation in colonoscopic surveillance programs have not.

**Methods:** We studied a previously described population-based cohort of 358 patients with left-sided (N = 151) or pancolonic (N = 207) ulcerative colitis who received care for at least 2 years within an integrated health care system and were eligible for screening colonoscopy based on duration of disease > 8 years. All procedures and pathology records were available electronically as part of clinical care. We determined 1) What proportion of patients underwent at least one screening/surveillance colonoscopy between 2001–2005; 2) what proportion of patients who underwent surveillance colonoscopy underwent a second surveillance within the recommended 1–2 years.

**Results:** Among 358 prevalent cases of UC eligible for screening/surveillance between 2001–2005, 123 (34%) underwent at least one surveillance colonoscopy during this time period. Among 123 patients who underwent one surveillance exam, 64 (52%) underwent an additional surveillance colonoscopy within the recommended 1–2 years. Overall, 64 of the 358 patients (18%) who were eligible for surveillance adhered to the recommended surveillance guidelines.

**Conclusion:** In an integrated health care system with access to colonoscopy, few patients with UC adhered to the recommended colonoscopic surveillance guidelines. If these guidelines represent the current standard of care, reasons for such poor rates of adherence must be further investigated. Furthermore, strategies to improve participation in colonoscopic surveillance must be developed.

## 1033

### Long-Term Efficacy of Adalimumab Treatment in Patients with Moderately to Severely Active Luminal Crohn's Disease Who Lost Response or Showed Intolerance to Infliximab

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*de Cabuenes, Gijón, Spain; Hospital de Galdakao, Vizcaya, Spain and On Behalf of GETECCU, Hospital Germans Trias I Pujol, Barcelona.*

**Purpose:** We evaluated the long-term efficacy and safety of adalimumab, a fully human monoclonal antibody against the tumor necrosis factor (TNF- $\alpha$ ), in the induction of clinical remission/response in patients with moderately to severely active Crohn's disease who lost response or showed intolerance to infliximab.

**Methods:** In this observational open-label multi-centre, prospective study, patients with moderate to severely active Crohn's disease (CDAI > 220) who had lost response or showed intolerance to infliximab were treated with subcutaneous adalimumab: 160 mg at week 0, 80 mg at week 2, then 40 mg every 2 weeks for 52 weeks. Subjects were assessed for clinical remission (CDAI < 150), clinical response (CR) 70 and CR100 (CDAI decrease of more than 70 or 100 points comparing with baseline) and safety.

**Results:** 38 patients were recruited who had luminal Crohn's disease (10 of them luminal fistulizing). Mean duration of CD was  $8.8 \pm 5.2$  years. At baseline, 55% were on AZA/6MP, 63% on corticosteroids, 42% had previous loss of response to infliximab, and 58% had developed intolerance to infliximab. The mean CDAI score at baseline was  $310.7 \pm 65.4$ . Long-term results are shown in the table.

**Conclusion:** Adalimumab treatment was effective in inducing and maintaining long-term clinical response and clinical remission in patients with moderately to severely active luminal Crohn's disease who had lost response or showed intolerance to infliximab. No new safety concerns were found compared with other adalimumab-treated populations.

## 1034

### Sustainability of Adalimumab in Fistula Healing and Response: 2-Year Data from CHARM and 12-Month Open-Label Extension Follow-Up Study

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**Purpose:** Adalimumab (ADA), a fully human monoclonal antibody that targets tumor necrosis factor, has been shown to be efficacious in the induction and maintenance of remission in patients (pts) with Crohn's disease (CD). Fistulizing disease complicates the course of CD in 20–30% of pts, in many cases leading to surgical resection. The CHARM study has previously shown efficacy of ADA in fistula closure and response. We assessed long-term efficacy of ADA in fistula healing and response in CD pts from the CHARM trial in an open-label extension (OLE) follow-up study.

**Methods:** Pts in CHARM were randomized to placebo (PBO), 40 mg every other week (EOW) or 40 mg weekly (EW). Pts with flare or non-response could receive OL ADA at/after Week 12. At the end of CHARM (56 weeks), pts were allowed to enroll into an open-label extension (OLE). In the OLE, pts received EOW OL or remained on EW OL, and could change from EOW to OL EW for flares or non-response. In this analysis, pts with fistulas at baseline (BL) of CHARM were studied, pooling the 2 doses, using an ITT, non-responder imputation analysis. Pts were analyzed for the percentage (%) of healed fistulas and % with  $\geq 50\%$  fistula response at 6 and 12 months in

Adalimumab Efficacy Over Time in Patients With Luminal CD

	Basal	Week 2 (N = 37)	Week 4 (N = 37)	Week 12 (N = 33)	Week 42 (N = 18)	Week 52 (N = 17)
CDAI (mean)	310.7	175.9	167.4	145.4	115.6	91.5
Remission (%)*(CDAI<150)	–	34.2	42.1	63.2	60.5	60.5
CR100* (%)	–	63.2	76.3	76.3	68.4	71.1
CR70* (%)	–	73.7	84.2	89.5	84.2	84.2

\*ITT-LOCF analysis

Long-Term Efficacy of Fistula Healing and  
Response with ADA Through 2 Years

Population	Endpoint	Month since baseline*	All ADA (EOW+EW combined)
% of pts with fistulas at BL of CHARM, (n/N)	Fistula healing	6	30 (21/70)
		12	33 (23/70)
		18	54 (38/70)
		24	51 (36/70)
% of pts with fistulas at BL of CHARM, (n/N)	≥50% Fistula response	6	46 (32/70)
		12	49 (34/70)
		18	70 (49/70)
		24	61 (43/70)

\*18 and 24 months represent 6 and 12 months of OLE after 12 months of blinded therapy in the CHARM study.

the blinded study and at 6 and 12 months of the OLE follow-up study (for a total of 24 months of therapy).

**Results:** Results are in the table below.

**Conclusion:** Sustainable efficacy of ADA in fistula healing and response is evident after 2 years. ADA has shown sustained response in almost two-thirds of the patients in the OLE who had fistulas at baseline of CHARM and sustained closure in more than half of the ADA-treated patients.

### 1035

#### Adalimumab Therapy for Patients with Ulcerative Colitis Who Have Lost Response or Are Intolerant of Infliximab

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**Purpose:** Adalimumab (ADA), a human antibody to tumor necrosis factor (TNF), is an effective treatment for patients with Crohn's disease who have lost response or are intolerant of infliximab (INF). We assessed the clinical response and adverse effects of adalimumab in patients with ulcerative colitis (UC) who have failed INF due to intolerance or loss of clinical response.

**Methods:** We queried the Inflammatory Bowel Disease Database at UCSF to identify all patients with a history of UC who were treated with ADA. The following data were retrospectively collected: patient demographics, clinical history, adverse events on IFX and ADA, and clinical response to therapy. Response to therapy was measured using the Simple Clinical Colitis Activity Index, where response was defined as a score of <5.

**Results:** Five patients (3 M/2 F) were identified with UC and treatment with ADA. The mean age was 29.6 [range 23–36] years, and 80% had pancolitis. All patients had duration of colitis of at least 5 years, and all were previously treated with INF. Three patients had an initial response to INF but eventually lost response despite 10 mg/kg every 4 week dosing, one patient never achieved a durable response to INF, and one patient had a severe infusion reaction in part due to episodic dosing of INF. One patient eventually responded to ADA after 11–12 weeks but required increased dosing to 40 mg weekly. One patient stopped ADA due to significant myalgias and fatigue. The remaining three patients failed to achieve a response to ADA and have been referred for colectomy.

**Conclusion:** ADA is well tolerated in patients with UC. Prospective studies in INF-naïve patients and past responders to INF are needed to determine its efficacy in this group.

## FUNCTIONAL BOWEL DISORDERS

### 1036

#### Predictors of Small Intestinal Bacterial Overgrowth in Patients with Irritable Bowel Syndrome

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**Purpose:** Patients with irritable bowel syndrome (IBS) have been associated with a higher prevalence of small intestinal bacterial overgrowth (SIBO) when compared to healthy controls. The aim of this study was to identify risk factors for SIBO in patients with IBS.

**Methods:** A total of 45 consecutive patients diagnosed with IBS who underwent hydrogen and methane breath testing for SIBO were identified retrospectively after excluding patients with other coexistent gastrointestinal and systemic disorders. Based on the referring physician substrate preference, 13 patients underwent glucose breath testing (GBT); 17 underwent lactulose breath testing (LBT); and 15 were given a combined glucose and lactulose solution. Among the 45 patients evaluated, 11 had positive breath tests (cases) and 34 had negative tests (controls). The cases and controls were compared with respect to age, duration of IBS symptoms, gender, predominant symptom, and Body Mass Index (BMI).

**Results:** Among the 45 patients with IBS who underwent breath testing, 11 (24.4%) had a positive test (5 with positive LBT, 5 with positive combined lactulose and glucose solution, and 1 had a positive GBT). A significant difference was seen in mean age and mean duration of symptoms in IBS patients with positive breath tests when compared to IBS patients with negative breath tests. In the multivariate analysis using ANCOVA, only duration of IBS symptoms remained statistically significant.

**Conclusion:** To our knowledge, this analysis is the first to evaluate age and duration of symptoms as a risk factor for a positive breath test in an IBS population. Our report suggests duration of IBS symptoms is independently associated with a significant risk for SIBO. Our results suggest it may be

**Table 1.** Patient data

Patient	Previous INF dose	Reason for stopping INF	ADA dose	Clinical response	Time to response	ADA adverse effects
1	10 mg/kg q4 weeks	Lost response	80 mg weekly	No		None
2	10 mg/kg q4 weeks	Lost response	40 mg weekly	Yes	11–12 weeks	None
3	10 mg/kg q4 weeks	Lost response	40 mg weekly	No		None
4	10 mg/kg q4 weeks	Lost response	40 mg every other week	No		None
5	5 mg/kg (episodic)	Severe infusion reaction	40 mg every other week	No		Myalgias, fatigue

more cost-effective to focus breath testing on those IBS patients with a longer duration of symptoms; however this needs to be evaluated in a prospective analysis.

Variable	Results		P value
	Positive Breath test	Negative Breath test	
Number	11/45	34/45	0.000000
Males	3/10	7/10	
Females	8/35	27/35	
BMI	28.6 ± 2.7	29.0 ± 1.2	0.655
Mean Age (years)	62.5 ± 3.3	51 ± 2.6	0.023
Median Age (years)	62	50	
Mean Duration of Symptoms (years)	25 ± 5.2	5.8 ± 1.4	<0.0001
Median Duration of Symptoms (years)	26	2	
Mean Age When Adjusted for Duration	58.07	51.57	0.254
Mean Duration When Adjusted for Age	23.5	6.3	0.000097

### 1037

#### Quality of Life (QOL) but Not Symptom Reporting Is Significantly Determined by Psychosocial Factors: Implications for Outcomes Endpoints

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**Purpose:** Health-related QOL and subjective reports of symptoms (sxs) are commonly assessed in both practice and research studies involving IBS pts. Previous studies demonstrate that psychosocial distress is frequently present in IBS and may influence both sxs and QOL. As the role of psychosocial factors in mediating sx and QOL in IBS remains incompletely defined, we sought to further clarify these relationships.

**Methods:** Rome II IBS pts were recruited through the NU GI Clinic and the internet. Pts completed an IBS specific QOL assessment (IBS-QOL) along with a GI sx measure (GISSI). Pts also completed measures of generalized anxiety and depression (HADS), measures of visceral-specific anxiety (Visceral Sensitivity Index; VSI), vital exhaustion (VE) and recent stressful life events (LE). Univariate analysis identified factors signif correlated with IBS-QOL and GISSI and these factors were then entered into regression analysis.

**Results:** 181 pts (mean (SD) age = 36(11); 88% F) were studied. With the exception of LE, all candidate variables were signif correlated with sx and QOL scores (Table). Stepwise regression of GISSI using signif correlated psychosocial variables identified only VE as a signif predictor ( $r^2 = 0.117$ ;  $P = 0.000$ ). Stepwise regression of IBSQOL total scores identified a 3-step model that included VSI ( $r^2 = 0.4$ ;  $P = 0.000$ ), VSI+HADS-D ( $r^2 = 0.53$ ;  $P = 0.000$ ) and VSI+HADS-D+GISSI ( $r^2 = 0.56$ ;  $P = 0.001$ )

**Conclusion:** In IBS, sx scores are not signif influenced by psychosocial factors with the exception of VE. QOL, however, is more signif influenced

by visceral anxiety and depression than by sxs. These data demonstrate that sx-based endpoints may be less confounded in clinical trials in IBS. These data also demonstrate that digestive sx anxiety and depression are more signif predictors of QOL in IBS than sxs. Optimizing clinical outcomes in IBS requires attention to these factors.

### 1038

#### Nightly Tegaserod Prevents the Clinical Recurrence of Bacterial Overgrowth Symptoms

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**Purpose:** We have recently demonstrated that antibiotic therapy improves IBS and is related to abnormalities on the lactulose breath test. We have further demonstrated a deficiency of migrating motor complexes (MMC) in IBS patients with an abnormal breath test. Based on a disturbed MMC, we test whether low dose erythromycin or tegaserod can prevent the recurrence of symptoms after successful antibiotic treatment.

**Methods:** In this study, a retrospective chart review was conducted on 203 consecutive patients seen in 2005 in the GI Motility Program. Patients were excluded if they did not have IBS, did not have a positive breath test, had an alternative diagnosis, or never had successful eradication of the abnormal breath test with clinical resolution. Those with clinical and breath test resolution were reviewed to determine the method of preventing symptom recurrence (none, erythromycin or tegaserod) and the time to recurrence with this method of prevention. Data was compared between groups as well as within groups if multiple methods were used on the same patient.

**Results:** Out of 203 patients, 64 patients had IBS, abnormal breath test, at least one successful treatment and follow up using a prevention strategy. Based on only the first successful antibiotic treatment, no preventive strategy ( $N = 6$ ) meant a recurrence of symptoms in  $59.7 \pm 47.5$  days compared to  $138.5 \pm 132.2$  days for erythromycin ( $P = 0.16$ ) and  $241.6 \pm 162.2$  ( $P = 0.01$  vs. none and  $P = 0.02$  vs. erythromycin). Any use of prevention was  $57.4 \pm 44.0$  for none,  $144.7 \pm 130.7$  for erythromycin ( $P = 0.04$  vs. erythromycin) and  $213.4 \pm 152.7$  days for tegaserod ( $P = 0.002$  vs. none and  $P = 0.02$  vs. erythromycin). In 18 patients after recurrence with erythromycin, tegaserod was used following antibiotic therapy. The number of days of prevention extended from  $102.7 \pm 67.8$  with erythromycin to  $224.3 \pm 159.2$  for tegaserod ( $P = 0.002$ ). 4 patients on no therapy were later given erythromycin or tegaserod and extended prevention from  $46.0 \pm 50.1$  to  $222.8 \pm 162.8$  days ( $P = 0.06$ ). Also, 2 patients stopped taking tegaserod prevention after 209 and 365 days of normal bowel function. After stopping tegaserod, symptoms recurred in 30 and 45 days respectively. 14 C-IBS patients used tegaserod as prevention ( $189.3 \pm 109.9$  days) and 16 D-IBS ( $278.6 \pm 197.4$  days,  $P = 0.13$ ).

**Conclusion:** Tegaserod is most effective in preventing relapse of clinical symptoms in IBS patients with positive breath test after antibiotic eradication. This work was supported by Novartis Pharmaceuticals.

### 1039

#### Methane Production in IBS Subjects Is Associated with a Constellation of Symptoms: Not Just Constipation

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	HADS-A	HADS-D	VSI	VE	LEQ	GISSI	IBS-QOL
Score (SDEV)	9.21 ± 4.55	6.69 ± 4.17	45.1 ± 16.36	21.71 ± 10.78	160.08 ± 104.14	91.53 ± 19.52	93.76 ± 28.44
GISSI (r; p)	0.18 (0.01)	0.31 (0.00)	0.3 (0.00)	0.34 (0.000)	0.13 (0.07)		0.44 (0.00)
IBSQOL (r; p)	0.43 (0.00)	0.61 (0.00)	0.63 (0.00)	0.59 (0.00)	0.08 (0.18)	0.44 (0.00)	

**Purpose:** Recent data are supporting a significant association between the presence of methane on lactulose breath test and constipation predominant IBS (C-IBS). In this study we aim to determine if methane is but one of an aggregate of GI symptoms that are typical of the methane producing IBS patient.

**Methods:** Consecutive IBS patients, referred for a lactulose breath test were prospectively enrolled in a database. Each patient was asked to complete a GI symptom questionnaire. Specifically, the symptoms inquired about the presence and degree of bloating, gas, abdominal pain, diarrhea, constipation, nausea, flatulence, urgency among others. The results of the lactulose breath test were also documented. The presence or absence of symptom was correlated between methane and non-methane producers. Since abdominal pain is a prerequisite for IBS, it was not compared.

**Results:** In the dataset, there were 458 patients with IBS of whom 72 (15.7%) were methane producers. In addition to constipation ( $P < 0.001$ ), methane producing subjects were more likely to have a greater degree of bloating ( $P = 0.053$ ), bloating with meals ( $P = 0.011$ ) and small bm's ( $P = 0.02$ ). In contrast, non-methane-producing IBS patients were more likely to have diarrhea ( $P < 0.0001$ ), fruit intolerance ( $P = 0.03$ ), weight loss ( $P = 0.011$ ), urgency ( $P = 0.013$ ) and dark stool ( $P = 0.043$ ).

**Conclusion:** Discrete differences in symptom complex exist between methane and hydrogen producing IBS subjects.

## 1040

### The Utility of Probiotics in the Treatment of Irritable Bowel Syndrome: A Systematic Review

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**Purpose:** To perform a systematic review of randomized controlled trials (RCTs) evaluating the efficacy, safety and tolerability of probiotics in the treatment of IBS.

**Methods:** Searches of MEDLINE, PUBMED, EMBASE and COCHRANE databases were performed to identify appropriate studies. Study selection criteria: (1) study design-randomized controlled trials (RCT); (2) study population-adults with IBS defined by Manning or Rome II criteria; (3) intervention-single or combination probiotic versus placebo; (4) outcome-improvement in IBS symptoms and frequency of adverse events. Data about quality of study design based upon Rome Committee recommendations was also extracted. Data were extracted in duplicate. Due to extreme variability in study design, study dosage, and outcome measures, quantitative pooling of data was not feasible.

**Results:** 13 RCTs met selection criteria. 11/13 studies demonstrated sub-optimal study design with inadequate blinding, inadequate trial length, inadequate sample size, and lack of ITT analysis. Only three studies provided any quantifiable data about tolerability and adverse events. The only probiotic to demonstrate significant improvement in IBS symptoms in appropriately designed studies was *Bifidobacterium infantis* 35624 (Align®, Procter & Gamble). In the first, *Bifidobacterium infantis* 35624 resulted in significant improvement in the composite score abdominal pain/discomfort, bloating/distention and bowel movement difficulty compared to placebo for the entire treatment period ( $P < 0.05$ ). In a subsequent study, *Bifidobacterium infantis* 35624 again demonstrated superior efficacy to placebo for the primary outcome measure abdominal pain/discomfort as well as the secondary measures bloating/distention, incomplete evacuation, straining, passage of gas and a composite score of abdominal pain/discomfort, bloating/distention, and bowel movement satisfaction at the a priori time point four weeks.

**Conclusion:** *Bifidobacterium infantis* 35624 has demonstrated efficacy for improvement in IBS symptoms. There is inadequate data to comment on the efficacy of other probiotics. Most trials do not provide adequate data about safety and tolerability. Future RCTs should follow Rome recommendations for appropriate design of an RCT and should provide precise data on tolerability and adverse events.

## 1041

### Tegaserod (Zelnorm) Safety Profile in Pediatric Patients

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**Purpose:** To evaluate for general as well as cardiovascular and neurologic ischemic side effects in pediatric pts prescribed tegaserod (Zelnorm). Zelnorm a selective 5HT<sub>4</sub> receptor agonist was used until recently as a prokinetic. 5HT<sub>4</sub> receptors are found throughout the GI tract and help regulate peristalsis, intestinal secretion, smooth muscle tone, and visceral sensitivity. FDA approval was in 2002 for the treatment of constipation predominant IBS in women and then in 2004 for idiopathic chronic constipation in men and women 18–65 yrs old. In March 2007, it was withdrawn from the market due to a statistically significant number of cardiovascular ischemic events in adult patients. The side effects of Zelnorm in the pediatric population have not been previously studied although it is used in many pediatric GI practices.

**Methods:** An IRB approved retrospective chart review was performed on 234 pts aged 21 and under prescribed Zelnorm. 133 charts had sufficient information for analysis.

**Results:** Indications for therapy were IBS 59.4%, chronic constipation 21.1%, GERD 6%, pseudo obstruction 10.5%, gastroparesis 10.5%, SMA syndrome 0.75%. 75.2% were female. Age range was 2–20 yrs (mean 14.4 yrs). Average duration of therapy was 146(range 2–1095) days. Most common complaints reported during therapy were abdominal pain (54%), continued constipation (31.6%), and nausea (23.3%). No pts had new onset neurologic deficits. 4 pts had cardiac symptoms; 2 of which had postural orthostatic tachycardia syndrome (POTS), 1 had panic attacks with anxiety disorder, and 1 had sinus bradycardia. All pts with cardiac symptoms had normal EKGs and no neurologic or cardiac side effects resulted in medication discontinuation. The most common reasons for discontinuation were completion of course 24.2%, diarrhea 19.7%, and no effect 19.7%.

**Conclusion:** Zelnorm has been prescribed in pediatric pts for a variety of indications. No cardiovascular or neurologic ischemic events were identified in any of the 133 pediatrics pts. Based on our data, Zelnorm appears to be safe for use in the pediatric population.

## 1042

### Male Sex Hormone May Influence on Irritable Bowel Syndrome in Young Men

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**Purpose:** The aim of the present study is to assess the sex hormone status of young male subjects with IBS and investigate whether there is any difference according to their predominant bowel symptoms.

**Methods:** Thirty eight young male patients with IBS were compared with 20 healthy young men. The symptom characteristics of patients were collected by interviewing with a structured questionnaire. The questionnaire inquired as to the duration, severity, and frequency of bowel symptom. Each subject had blood test, stool examination, and colonoscopy were performed to rule out the organic intestinal diseases.

Blood test included serum testosterone, free testosterone, sex hormone-binding globulin (SHBG), follicle stimulating hormone (FSH), and luteinizing hormone (LH). On the basis of the questionnaire, patients with IBS were classified as two groups; diarrhea-predominant (IBS-D) and constipation-predominant (IBS-C) groups.

**Results:** Among 38 patients with IBS, 24 patients were IBS-D and 14 patients were IBS-C. Patients with IBS had lower levels of testosterone and SHBG than control ( $P = 0.04$  and  $P = 0.03$ , respectively). However, there was no significant difference between IBS-D group and IBS-C group in Testosterone

and SHBG. Levels ( $P > 0.05$ ). In addition, there was no difference in duration and severity of symptom between IBS-D group and IBS-C group ( $P > 0.05$ ). **Conclusion:** Sex hormonal status in young men may play a role in the pathophysiology of IBS regardless of dominant symptom type. Further exploration of the role of male sex hormones in IBS is needed.

## 1043

**A Long-Term Follow-Up Study of Children with Chronic Constipation**  
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**Purpose:** 1. Determine the outcome of CIC 10–15 years later. 2. Determine the social, educational and occupational functioning in children with CIC. 3. To determine the factors influencing the outcome in childhood CIC.

**Methods:** Retrospective chart review followed by a telephone interview. A total of 560 charts with CPT code for idiopathic constipation, seen between 1985–95, were randomly chosen and reviewed. 231 subjects met our inclusion/exclusion criteria. Initial data was collected from these 231 subjects and a follow-up questionnaire was sent to all of these subjects, 2 weeks prior to telephone contact. A total of 73 (31.6%) subjects have responded when contacted by telephone.

**Results:** Mean age at initial presentation and f/u data collection were 5.3 and 22.4 years, respectively. A slight male preponderance was noted both at the initial presentation and f/u (54% vs. 46% and 60% vs. 40%). More than 70% of subjects had problems with abdominal pain, stool impaction, large/hard stools, painful defecation and stool withholding at initial presentation. However, at 10–15 years f/u, abdominal pain, painful defecation, rectal blood loss and hard stools were rare (all  $P < 0.001$ ). But 6% of the subjects reported to have constipation and 18% of the subjects admitted to having at least one symptom of constipation. About 6% of the subjects were still taking at least one type of treatment and another 6% of the subjects reported to have significant impairment in social, educational or occupational functioning. Preliminary analysis shows that male sex was the only factor that influenced the persistence of constipation at 10–15 years f/u.

**Conclusion:** CIC in childhood is a common condition that can persist even 10–15 years after initial presentation. About 6% of the subjects reported to have constipation and 18% of the subjects continued to have at least one symptom of constipation even 10–15 years after initial presentation. More importantly, 6% of the subjects reported to have significant impairment in social, educational or occupational functioning. Male sex may predispose to the persistence of this condition into adulthood. Given the current prevalence of this condition in children, development of an effective long-term intervention plan is recommended.

## 1044

**Self-Perceived Stigma in IBS: Relationship to Quality of Life, Self-Efficacy, Self-Esteem, and Psychiatric Distress**

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**Purpose:** Half of IBS pts report feeling stigmatized with stigma severity influenced by both degree of role limitations and the extent to which pts feel their diagnosis is not regarded by themselves or others as a credible explanation for role limitations (Gastroenterol 2007;132:A521). In other disorders, stigma is assoc with poorer quality of life and psychiatric distress. This has not been studied in IBS. We recently developed and validated a measure of perceived stigma in IBS. This study examined the relationship between relevant psychosocial constructs and stigma in IBS.

**Methods:** 67 pts with an established diagnosis of Rome II IBS were studied (age =  $51 \pm 15$  yrs; 57 F/10 M). Pts completed a measure of IBS-related perceived stigma along with measures of QOL (SF-12) and psychiatric distress (BSI). The SF-12 reports QOL related to physical (PCS) and mental function (MCS). The BSI includes scales for anxiety (BSI-A), depression (BSI-D) and somatization (BSI-S) as well as a global symptom index (GSI). Pts also completed HADS and measures of self-efficacy (EFF; Perceived Self-Efficacy Scale) and self-esteem (EST; Rosenberg Self-Esteem Scale).

**Results:** Perceived stigma was not influenced by age or gender. Increasing levels of perceived stigma were assoc with poorer QOL on MCS ( $r = -0.29$ ;  $P = 0.04$ ) but not PCS scales ( $r = -0.07$ ;  $P = 0.63$ ). Increasing stigma was assoc with increasing psychiatric distress on BSI-A ( $r = 0.40$ ;  $P = 0.01$ ) and BSI-S ( $r = 0.31$ ;  $P = 0.01$ ) but not BSI-D ( $r = 0.2$ ;  $P = 0.11$ ). Increasing stigma was assoc with higher HADS-Anx ( $r = 0.4$ ;  $P = 0.001$ ) and HADS-Dep ( $r = 0.38$ ;  $P = 0.002$ ) scores. Perceived stigma was also assoc with poorer EFF ( $-0.29$ ;  $0.02$ ) and lower EST ( $-0.43$ ;  $0.00$ ). Stepwise regression identified only EST as a significant predictor of stigma ( $r^2 = 0.19$ ;  $P = 0.00$ ).

**Conclusion:** Increasing levels of self-perceived stigma in IBS are assoc with poorer QOL, psychiatric distress, poor self esteem and poor self-efficacy. However, regression analysis identifies only low self-esteem as a significant predictor of perceived stigma. These data are consistent with prior studies identifying self-blaming, isolation and lack of diagnostic validity as important stigma determinants. Evaluation of IBS pts should include queries regarding perceived stigmatization as well as psychiatric distress.

## 1045

**A Randomized, Controlled, Double-Blind Trial of s-Pindolol in Irritable Bowel Syndrome (IBS)**

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**Purpose:** Pindolol is a synthetic beta-adrenergic receptor blocking agent with intrinsic sympathomimetic activity which exists as a racemic mixture of the R and S enantiomers. The R and S enantiomers of pindolol differ in both their pharmacokinetics and pharmacodynamics. The beta-adrenoceptor blocking effects of pindolol are largely confined to the S enantiomer, while the intrinsic sympathomimetic activity is shared equally by the R and S enantiomers. In addition, 5HT<sub>1A</sub> antagonism is a property of s-pindolol. Given these properties and our current understanding of IBS, our aim was to evaluate the efficacy of s-pindolol in IBS.

**Methods:** Following a 8–14 day run-in period, eligible patients were randomly allocated to s-pindolol 2.5 mg t.i.d or placebo t.i.d. for four weeks. Patients receiving s-pindolol then had dose adjusted to 5 mg t.i.d for a further four weeks and to 7.5 mg t.i.d for the final four weeks, if tolerated. Three primary endpoints: Difference in the percentage of responders between AGI-001 and placebo based on 1. patient's global impression and 2. relief of abdominal pain/discomfort; 3. use of rescue medication (paracetamol). Numerous secondary endpoints were also assessed. The pre-defined statistical analysis was a one-sided analysis based on the hypothesis that s-pindolol is better than placebo.

**Results:** There was no difference between treatments in terms of the number of patients who felt better on at least 50% of study days (one-sided  $P = 0.30$ ). Logistic regression analysis yielded an odds ratio for AGI-001 relative to placebo: 0.73 (95% C.I. 0.24–2.20). The proportion of days of adequate relief of abdominal discomfort/pain did not differ between treatments (one-sided  $P = 0.34$ ); odds ratio for AGI-001 relative to placebo: 0.77 (95% C.I. 0.25–2.42). Use of paracetamol was sparse and similar in both groups (one-sided  $P = 0.11$ ). There were significant s-pindolol related improvements compared to baseline in the secondary endpoints of global severity of illness, abdominal pain, bloating/distention and straining at the highest dose visit (week 12). The incidence of adverse events was similar in s-pindolol- and placebo-treated groups.

**Conclusion:** In this IBS study we have failed to reveal a significant benefit for s-pindolol at the doses administered in terms of global relief of IBS symptoms, relief of abdominal pain, or use of rescue medication.

## 1046

#### A Randomised, Double-Blind, Placebo-Controlled Study of r-Verapamil in Non-Constipated Irritable Bowel Syndrome

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**Purpose:** IBS is a common and clinically challenging gastrointestinal disorder for which few therapies of proven value are available for clinical use. Since the r-enantiomer of verapamil (r-verapamil) has been found to have a unique combination of activity not involving 5HT<sub>3</sub> or 5HT<sub>4</sub> and has been shown to have highly selective activity on the gastrointestinal tract compared to the cardiovascular system, the aim of this study was to assess the efficacy and safety of r-verapamil in the treatment of IBS.

**Methods:** 129 male or female patients who fulfilled Rome II criteria for non-constipation predominant IBS were randomised to placebo (N = 64) or to r-verapamil (N = 65). R-verapamil was administered in an ascending dose schedule from 20, 40, to 80 mg t.i.d. across all r-verapamil treated patients. Dose escalation occurred at 4-week intervals; the entire treatment period was 12 weeks. The primary efficacy variables were the responder rates for patient global impression and relief of abdominal pain/discomfort which in turn were defined as feeling better on at least 50% of the entire 42 study days. The pre-defined statistical analysis was a one-sided analysis based on the hypothesis that r-verapamil is better than placebo.

**Results:** 14 patients discontinued prematurely, 6 in the r-verapamil and 8 in the placebo group. Analysis of the intention-to-treat (ITT) population for the primary efficacy variables revealed significantly higher responder rates for r-verapamil for both the patient global impression (56.9% vs 37.5%, one-sided  $P = 0.0057$ ) and abdominal pain/discomfort (56.9% vs 43.8%, one-sided  $P = 0.05$ ). Significant benefits for r-verapamil were also evident for several secondary endpoints: composite GI symptom scale, bloating, stool frequency, urgency, Bristol stool scale and quality of life, as measured by the IBS-QOL. Adverse events were experienced by 17 patients in the r-verapamil and 8 in the placebo group. No severe AEs were recorded with the AE profile being very similar to the reported AE profile for racemic verapamil. Only 4 patients reduced their dose because of an AE.

**Conclusion:** R-verapamil appears to be effective and well tolerated in the management of patients with non-constipation predominant irritable bowel syndrome given the significant response seen in the two primary and numerous secondary endpoints.

## 1047

#### Predictors of Better Quality of Life Outcomes in Patients Suffering from IBS

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**Purpose:** Abdominal pain/discomfort, bloating and constipation are gastrointestinal (GI) symptoms related with irritable bowel syndrome (IBS). These symptoms are associated with impaired quality of life and work productivity. LOGIC (Longitudinal Outcomes Study of GI Symptoms in Canada) has been conducted as a prospective, observational study designed to evaluate the treatment patterns and health outcomes of patients with IBS symptoms in Canada.

**Methods:** The study was designed to characterize the clinical characteristics, quality of life (IBS-QOL), healthcare resource utilization and productivity

of patients with symptoms associated with IBS over a 1-year period. A total of 1556 subjects were enrolled at 147 centers across Canada. The present analysis employed a multivariate logistic regression model to identify predictors associated with better IBS-QOL outcomes: subjects were declared to have had a "better outcome" if they were in the top 25% of the baseline to month 12 change scores, (i.e., a 13 point increase in IBS-QOL in this study).

**Results:** A total of 1035 subjects with complete data were included for this logistic regression analysis. It showed that baseline IBS-QOL score ( $P < 0.001$ ), usage of tegaserod\* (i.e., subject reported taking  $> 7$  days or  $> 7$  tablets of tegaserod in the first month;  $P = 0.006$ ) and type of insurance (public, private, both or none,  $P = 0.030$ ) were significant predictors. The effects of IBS subtype (IBS-C, IBS-D or IBS-A;  $P = 0.055$ ) and employment status ( $P = 0.082$ ) were marginally significant, and age, gender, level of education, number of prior specialist visits, use of prior pain medication and disease severity were not significant. A more detailed analysis showed a significantly increased probability for better outcomes ( $OR = 2.0292$ ,  $P = 0.0023$ ) among tegaserod treated subjects if they were untreated in the past and lower baseline IBS-QOL scores increased the chance of a better outcome ( $OR = 0.691$  per 10-point increase in baseline IBS-QOL score).

**Conclusion:** Baseline IBS-QOL score, tegaserod use and insurance type play major roles as predictors influencing the quality of life outcomes of patients suffering from irritable bowel syndrome. \*Please note that at Health Canada's request, as of March 30, 2007, Novartis Pharmaceuticals Canada Inc. has suspended the marketing and sales of Zelnorm (tegaserod) in Canada.

## 1048

#### Expression of P2X Receptor in a Rat Model of Chronic Visceral Hyperalgesia

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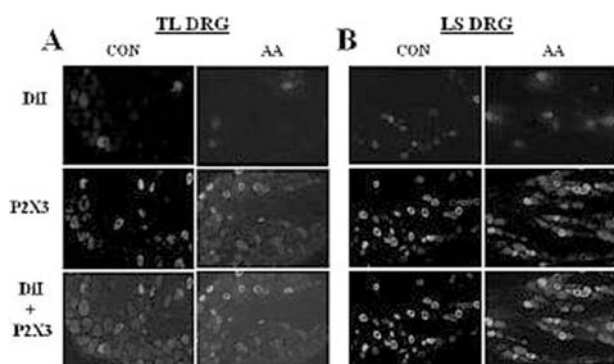
**Purpose:** Chronic visceral hypersensitivity (VH) is an established phenomenon in patients with irritable bowel syndrome (IBS) suggesting sensitization of nociceptive pathways. Recent studies suggest a role of purinergic signaling mediated by the P2X receptor family in VH. P2XRs are non-selective cation-permeable ion channels, gated by extracellular ATP and predominantly expressed by nociceptive dorsal root ganglion (DRG) neurons.

Our previous experiments on the rat model of IBS-like visceral hyperalgesia have shown that antagonism of P2XRs by TNP-ATP attenuates the behavioral nociceptive responses to mechanical stimulation of the colon in hypersensitive rats but not in controls. **The aim of this study was to determine if the expression of P2×3Rs in colonic sensory neurons was increased in rats with colonic hyperalgesia.**

**Methods:** Ten days old rat pups received a colorectal infusion of 0.5% acetic acid (AA) in saline or saline alone (controls). At 8–12 weeks AA sensitized rats displayed an increased sensitivity to colorectal distension & excitability of colon-specific DRG neurons in the absence of structural or inflammatory changes in the colon. Colon specific DRG neurons labeled by injecting lipid soluble fluorescence dye (DiI) into rat colon. Sections from dissected out T13-L2 & L6-S2 DRGs were stained with primary antibodies (anti-P2×3 receptors) and then fluorescent secondary antibody. Sections viewed under BX60 Olympus microscope equipped with appropriate filter. Images were analyzed with Metaview software. Neurons colabeled with DiI and P2×3 were counted for both groups (see Figure).

**Results: Percentage of P2×3 positive colon specific DRG neurons** Thoraco-Lumbar: 18% for AA treated rats vs. 5% in controls,  $P < 0.05$  Lumbo-Sacral: 56% in AA treated group vs. 28% in controls,  $P < 0.05$

**Conclusion:** Colon specific sensory afferent neurons from AA sensitized rats show an up regulation of P2X receptors. Thus we conclude that **up regulation of P2XRs is associated with chronic colorectal allodynia and hyperalgesia in this model.** This up-regulation may explain the efficacy of the P2×3 antagonist in sensitized rats but not in controls.[figure1]



1049

### Do Autonomic Function and $\alpha_2$ Adrenergic Genotypes Predict IBS Phenotype?

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**Purpose:** Autonomic nervous system (ANS) dysfunction may play a role in irritable bowel syndrome (IBS). Most previous studies examined small numbers of patients and came to disparate conclusions. Our aim was to clarify whether autonomic function and candidate genes controlling  $\alpha_2$  adrenergic receptors predict the IBS phenotype.

**Methods:** Using Rome II criteria for IBS, 87 patients were subclassified as constipation (C)- or diarrhea (D)- predominant, or mixed (M) IBS. There were 36 controls. Autonomic function was determined by three sympathetic adrenergic [change in systolic (S) and diastolic (D) blood pressure (BP), plasma norepinephrine (NE) at 1 min standing, Valsalva ratio] and one vagal [heart rate (HR)] measurements. Associations between phenotype, ANS and genotypes were tested using logistic regression models to predict phenotype adjusted for age, body mass index (BMI) and depression/anxiety scores, and using multiple linear regression models to predict ANS using genotype adjusted for age and BMI.

**Results:** Clinically similar mean ANS test results were observed among IBS subgroups and controls (table, mean  $\pm$  SEM). There was no significant association between autonomic function and IBS phenotype. The odds ratio (95% CI) for C-IBS was modestly increased in subjects with  $\alpha_{2A}$  adrenergic GG/CG genotype [OR = 2.5 (0.9, 1.3),  $P = 0.09$ ] while no significant association was detected for  $\alpha_{2C}$ . However  $\alpha_{2C}$  adrenergic genotype modestly influenced DBP response to standing while  $\alpha_{2A}$  did not appear to be associated with ANS response.

**Conclusion:** Autonomic function and  $\alpha_{2C}$  adrenergic genotype do not appear to predict IBS phenotype; the association of  $\alpha_{2A}$  adrenergic genotype and IBS-C confirms the potential role of adrenoceptor control as a factor in IBS, but this is not mediated through systemic adrenergic modulation.

	n	$\Delta$ SBP mmHg	$\Delta$ DBP mmHg	$\Delta$ NE pg/ml	$\Delta$ HR/min
Controls	36	3.0 $\pm$ 1.2	-5.6 $\pm$ 1.1	154 $\pm$ 21	15.9 $\pm$ 1.7
IBS total	87	1.2 $\pm$ 0.9	-6.1 $\pm$ 0.9	174 $\pm$ 11	13.5 $\pm$ 1.4
IBS-C	33	3.1 $\pm$ 1.3	-5.9 $\pm$ 1.8	189 $\pm$ 20	15.2 $\pm$ 2.4
IBS-D	30	1.8 $\pm$ 1.5	-3.6 $\pm$ 1.4	152 $\pm$ 19	11.6 $\pm$ 2.3
IBS-M	24	-2.0 $\pm$ 1.8	-9.3 $\pm$ 1.3	183 $\pm$ 16	13.5 $\pm$ 2.5
$\alpha_{2C}$ wildtype	107	1.7 $\pm$ 0.8	-5.6 $\pm$ 0.8	162 $\pm$ 11	13.5 $\pm$ 1.2
$\alpha_{2C}$ non-wildtype	8	3.4 $\pm$ 2.6	-9.8 $\pm$ 2.8	202 $\pm$ 40	17.0 $\pm$ 4.7

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### Colonic Diverticular Disease and Diarrhea-Predominant Irritable Bowel Syndrome: An Etiological Link?

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**Purpose:** Colonic diverticular disease is common, and many of them report unexplained lower GI symptoms. Some have attributed these symptoms to irritable bowel syndrome (IBS), but whether IBS and diverticular disease are causally linked is uncertain. We aimed to evaluate this association in a representative population-based case-control study.

**Methods:** A population-based, cross-sectional survey was conducted by mailing a valid symptom questionnaire to eligible residents of Olmsted County, MN, aged 30–95 years. IBS was defined by Rome II. Colonic diverticular disease was ascertained through complete medical record abstraction of all responders. Subjects with at least one colon test (barium enema, colonoscopy, or CT colonography) were included.

**Results:** Among 2298 subjects (55% response rate), there were 1784 respondents with colon tests (78%): 959 women (54%); mean ( $\pm$  SD) age 65 ( $\pm$  12). Colonic diverticular disease was identified in 43.1% (95% CI 40.7–45.4). Older age ( $\geq 60$  years) was a significant predictor for diverticular disease (OR 2.21, 95% CI 2.00–2.44), but no association with gender was detected. Overall, IBS was reported by 8.1% (95% CI 6.3–10.2) of men and 15.0% (95% CI 12.8–17.4) of women. After adjusting for age and gender, the presence of IBS was significantly associated with an increased odds for diverticular disease (OR 1.80, 95% CI 1.30–2.50). Relative to the non-IBS subgroup, diarrhea (D)-IBS and alternating (A)-IBS had significantly increased odds for diverticular disease (OR 2.01, 95% CI 1.14–3.53 and OR 2.65, 95% CI 1.19–5.93, respectively); constipation (C)-IBS was not associated. After adjusting for age and gender, higher somatic symptom score, abdominal pain relieved by bowel movement, diarrhea, lower abdominal pain and bloating were also each significantly associated with diverticular disease, while smoking, alcohol, marital status, education, and body mass index were not associated.

**Conclusion:** There is a significantly increased frequency of colonic diverticular disease in subjects with D- and A-IBS in a US community, but not C-IBS. The results suggest that D-IBS and colonic diverticular disease may be etiologically connected, perhaps via localized inflammatory change.

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### Risk Factors for Chronic Diarrhea Not Related to Irritable Bowel Syndrome

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**Purpose:** The prevalence of chronic unexplained diarrhea in the community has not been well established, but many cases are presumably due to irritable bowel syndrome (IBS). Risk factors for functional diarrhea in the absence

of IBS are unknown. The objective of this study was to evaluate potential risk factors for chronic unexplained diarrhea in the community excluding IBS.

**Methods:** A valid self-report questionnaire that recorded gastrointestinal symptoms required for a diagnosis of chronic diarrhea, self-reported measures of potential risk factors, and a somatic symptom checklist (SSC) was mailed to an age- and gender- stratified random sample of Olmsted County, Minnesota residents aged 30–64 yr. Chronic diarrhea was defined as having one or more of the following symptoms: three or more bowel movements a day, loose or watery stools, or fecal urgency. Subjects with symptoms of IBS based on the Rome criteria were excluded. Univariate logistic regression models and models that adjusted for age, gender, and SSC score were used to identify factors associated with chronic diarrhea and compute Odds Ratios (OR) [95% Confidence Intervals]. These models were examined using all subjects not reporting IBS, and separately, the subset with no abdominal pain.

**Results:** Of the 892 eligible subjects, 653 (73%) returned the survey. Among the 523 respondents not reporting IBS, chronic diarrhea was reported by 148 (28%) subjects; 58 (39%) reported abdominal pain while 90 had chronic painless diarrhea. Chronic diarrhea was significantly associated with food allergy (OR = 2.05[1.31–3.20]) and stress (OR = 1.99[1.03–3.85]), but the latter association was attenuated in the model adjusted for covariates. Both remained significant in the adjusted variable models that excluded subjects with any abdominal pain. Female gender (OR = 0.67[0.45–0.98]) and higher education level (OR = 0.60[0.39–0.92]) were factors with significantly smaller odds for chronic diarrhea. No association was detected for age, marital status, body mass index, cigarette or alcohol use, coffee, analgesics, emotional support, pets, or water source.

**Conclusion:** Chronic diarrhea not related to IBS is common and most have no abdominal pain; food allergy, male gender and a lower level of education are risk factors. The etiologic role of these factors requires further investigation.

## 1052

### Work Productivity Is More Impaired in Functional Gastrointestinal Disorders Compared to GERD: Six-Month Data from PROGRESS

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**Purpose:** To assess work productivity and activity impairment over six months in patients with functional GI disorders (FGIDs), including irritable bowel syndrome with constipation (IBS-C), chronic constipation (CC), and functional dyspepsia (FD), compared to patients with gastroesophageal reflux disease (GERD).

**Methods:** The Patient Registry for Observational Gastrointestinal Research Epidemiology and Symptom Severity (PROGRESS) enrolled patients with one of the following GI conditions: IBS-C, CC, FD, or GERD,

as confirmed by their primary care physician. The validated Work Productivity and Activity Impairment questionnaire, adapted for GI diseases (WPAI:GI), was administered biweekly between April 2005 and April 2006. Scores were expressed as percent of impairment/productivity loss resulting from GI disorders (higher scores indicate greater impairment and less productivity).

**Results:** 161 FGID (86 IBS-C, 39 CC, 36 FD) and 239 GERD patients were enrolled. Surveys yielded mean response rates between 46% and 66% for each of the WPAI categories. Mean age was 51 years, 69% of patients were women, 82% were Caucasian, and 67% worked at least parttime at baseline. FGID patients reported greater work and daily activity impairment than patients with GERD (Table 1).

**Conclusion:** Patients diagnosed with a FGID, such as IBS-C, CC, or FD, reported greater work productivity loss and daily activity impairment over a six-month period compared to patients with GERD. This impairment amounts to the loss of at least one day of work in a 40-hour workweek.

## 1053

### Transition of Gastroesophageal Reflux Disease Symptoms into Other Gastrointestinal Symptoms: Six Month Prospective Study

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**Purpose:** To assess the transition of gastroesophageal reflux disease (GERD) symptoms into chronic constipation (CC), diarrhea, and/or dysmotility symptoms in patients with GERD.

**Methods:** 239 GERD patients were enrolled into the Patient Registry for Observational Gastrointestinal Research –Epidemiology and Symptom Severity (PROGRESS). Symptom frequency was assessed bi-weekly for 6 months using a symptom assessment survey developed and validated for this study. 4 symptom scales were identified: CC, diarrhea, dysmotility, and reflux. Scale scores range from 0 to 100 (higher scores: increasing severity). Trend lines for all symptom scales were created for each patient using ordinary least squares. A 'transition' was defined as an increase in the slope of the trend line of a non-GERD symptom score combined with a decrease in the slope of the trend line of the GERD symptom score. Means were calculated for 'transition' patients in 3 scores: beginning, middle (average of 2 middle scores used if even # of surveys completed), and end (score from last survey completed), and were compared using ANOVA.

**Results:** GERD patients included in the analysis (N = 229) had a response rate of 73%. Mean age was 52 yrs, 65% of patients were women, and 83% were Caucasian. In this population, 28% (N = 63) of patients with a diagnosis of GERD met the transition definition. Over the study period, 14% (N = 31) of GERD patients experienced a transition to CC, 16% (N = 36) to diarrhea, and 15% (N = 34) to dysmotility. GERD scores decreased over time (Table 1).

**Table 1.** Mean WPAI Scores in GERD vs FGID Patients Over Six Months

WPAI Categories	GERD	FGID			
		TOTAL	IBS-C	CC	FD
Work time missed	2.7 (1.2)	4.1 (2.6) <i>P</i> = .06	3.9 (3) <i>P</i> = .53	3.9 (2.9) <i>P</i> = 1	5.2 (4.2) <i>P</i> = .23
Impairment at work	14.1 (2.6)	23.8 (3) <i>P</i> < .001	24.4 (3.2) <i>P</i> < .001	21.9 (6.5) <i>P</i> = .03	25.3 (7.6) <i>P</i> = .26
Work productivity loss	15.8 (3.4)	25.8 (3.8) <i>P</i> < .001	25.9 (4.3) <i>P</i> = .003	23.8 (6.3) <i>P</i> = .14	28.6 (8.2) <i>P</i> = .05
Hours lost per week†	6.3	10.3	10.4	9.5	11.4
Daily activity impairment	16.8 (2.2)	24.5 (3) <i>P</i> < .001	25.7 (3) <i>P</i> = .01	26 (4) <i>P</i> = .05	20.5 (5.8) <i>P</i> = 1

\*Significant *P*-values indicate significant differences between FGID cohort and GERD cohort † Assumes a 40-hour workweek

Mean Scores (s.d.)/*P*-value\*



**Table 1.** Mean (sd) Symptom Scale Scores at Beginning, Middle, & End of Study

Transition Symptom	CC		Diarrhea		Dysmotility	
	CC	GERD	Diarrhea	GERD	Dysmotility	GERD
Beginning	15.7 (18.2)	25.5 (15)	16.2 (15.7)	31.4 (21.9)	20.4 (17.9)	28.8 (17.5)
Middle	18.4 (15)	17.6 (15.2)	21.2 (18.2)	17.9 (17.3)	24.1 (19.1)	18.1 (17.1)
End	18.5 (17.4)	11.3 (11.5)	25.2 (20.6)	14.4 (14.4)	28 (20.9)	15.6 (17.3)
P-value	0.46	0.001*	0.13	0.001*	0.23	0.004*

\*Significant difference in mean scores for transition patients

**Conclusion:** Patients with GERD often will have symptom transition toward a GI dysmotility and sensory disorder. Further research should be done to establish a common gastrointestinal precursor to GERD and GI dysmotility.

## 1054

### Development and Validation of the Bloating Symptom Impact Scale (B-SIS)

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**Purpose:** Bloating is both common and bothersome in GI patients and has been associated with increased healthcare utilization. Bloating can be present in isolation, but is frequently a symptom associated with IBS and/or functional dyspepsia. Several disease-specific QOL measures are available to assess the impact of IBS and functional dyspepsia, but currently no bloating-specific QOL instrument has been validated.

**Aim:** To develop and validate a new, multi-dimensional, bloating-specific scale to assess the impact of bloating on HRQOL in patients with FGIDs.

**Methods:** Initially, 22 items were derived from focus groups, literature review, professional experience and face validity. The survey was administered to 122 GI out-patients with FGIDs. Principal Component Analysis (PCA) with Varimax rotation and Kaiser Normalization (SPSS v14) was completed. The number of components was determined by the total explained variance, simple structure, and eigenvalues > 1. The final subscales were comprised of item loading exceeding 0.40 with a particular component, while minimizing cross-loadings. Test-retest was assessed from 20 patients and controls who completed the survey twice about 2 wks apart. Internal consistency was assessed according to Cronbach's alpha. Validity was assessed by comparing domains of the B-SIS with SF-12 domains.

**Results:** The initial PCA suggested a five-component solution for the total sample, but simple structure was best derived from 4 components: "Physical Role" (58.5%), "Social Role" (10.1%), "Emotional" (6.8%), and "Ingestive Behavior" (4.3%). Seven items demonstrated complex interactions with multiple components or failed to contribute significantly and were deleted. The final questionnaire included 15 items and accounted for 80% of total variance. Cronbach's alpha ranged from 0.87–0.93 for the subscales, supporting good internal consistency. Test-retest reliability was adequate and ranged from 0.55 – 0.95. Acceptable concurrent validity was demonstrated.

**Conclusion:** The B-SIS demonstrated excellent psychometric qualities and provides a validated, multi-dimensional, bloating-specific scale to assess the impact of bloating symptoms on HRQOL in patients with FGIDs.

## 1055

### From Mouse Knockout to Investigational Drug: LX1031, a Novel Potential Treatment for Irritable Bowel Syndrome

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**Purpose:** Peripheral serotonin (5-HT) plays a critical role in the modulation of intestinal motility and nociception. 5-HT is also associated with functional gastrointestinal disorders (FGID) such as irritable bowel syndrome (IBS). Its synthesis in the gastrointestinal (GI) tract is initiated by the enzyme tryptophan hydroxylase type I (TPH1) located in the enterochromaffin (EC) cells. Pharmacological inhibition of TPH1 can reduce GI serotonin levels and may provide treatment for IBS and other FGIDs.

**Methods:** Using gene knockout (KO) technology, the tph1 gene was functionally deleted in the mouse. Mice lacking tph1 were viable and healthy. Importantly, brain 5-HT, which is produced by a second isozyme of tph, tph2, was maintained at normal levels. A small molecule inhibitor of TPH1, LX1031, was discovered and developed. When administered orally to rodents for up to five days, LX1031 reduced intestinal 5-HT levels dose dependently without affecting brain 5-HT levels, effectively recapitulating the KO phenotype. LX1031 inhibits the TPH1 enzyme in the EC cells of the GI tract without significant systemic exposure, thus reducing the potential for side effects. Preclinical studies of LX1031 revealed an excellent safety profile supporting the initiation of human clinical trials.

**Results:** In a randomized, double-blind, single ascending dose study, LX1031 was well tolerated by healthy subjects at all doses given. The pharmacokinetic behavior of the compound was consistent with preclinical observations with a low C<sub>max</sub> ranging from 75 ng/mL at 250 mg to 141 ng/mL at 1500 mg in fasted subjects with exposure saturation suggested beginning around 500 mg. In a cross-over study, after a 6-day washout, the 1000 mg cohort showed 2-fold increased exposure when dosed following a high fat meal. T<sub>max</sub> was achieved after approximately 4–5 hours for all fasted dose groups and was slightly delayed with food, at 6 hours. Treatment emergent adverse events were infrequent at all dose levels with no consistent findings by dose or event type and none were considered related to LX1031.

**Conclusion:** Genetic analysis of tph1 KO mice and preclinical studies of LX1031 indicate tph1 inhibition may provide a novel route to safely modulate GI 5-HT levels. Initial clinical studies indicate that single doses of LX1031 are well tolerated up to 2000 mg with low systemic exposure. Multidose studies are ongoing to assess the pharmacodynamic effects of LX1031 on the whole blood 5-HT and urinary 5HIAA (a 5-HT metabolite) biomarkers.

## 1056

### Functional Dyspepsia: The Economic Impact to Patients

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**Purpose:** Functional dyspepsia (FD) is a highly prevalent disorder that results in significant financial burden to the health care system. Little is known about the economic impact of FD to patients. The aims of this study were to use a validated questionnaire to quantify FD patients' health care utilization patterns and to estimate direct and indirect costs of FD to patients.

**Methods:** ICD-9 codes identified patients (≥18 years) with dyspepsia. Charts were individually reviewed to confirm patients met Rome III criteria for FD, and to document a normal upper endoscopy. A validated questionnaire was mailed to patients meeting these criteria. Responses were anonymous. Data was analyzed using SPSS statistical software.

**Results:** 297 patients met inclusion criteria, and 178/297 (60%) responded. The respondents' mean age was 51 ( $\pm 14$ ) years; 75% were women, 87% were Caucasian, and 16% earned more than \$50,000 (US) per year. Respondents had a mean of 8 ( $\pm 8$ ) years of FD symptoms, which were self-rated as moderate (52%) or severe (20%). Patients reported a mean of 3 visits to the primary care clinic over the last 12 months. To further evaluate their FD symptoms, 95% reported having had blood work, 92% an EGD, 59% an ultrasound, and 40% a CT scan. In this patient subset, the direct cost of testing based upon the national Medicare reimbursement rate per patient is \$621. To improve their FD symptoms, 92% made dietary changes, 89% used over-the-counter (OTC) medications, 88% used prescription medications, 25% tried alternative therapies, and 10% had seen a counselor. 18% of respondents reported having been hospitalized at least once in their lifetime for FD and 23% reported having had a surgery. Mean patient expenditure over the last year was \$246 for OTC medications (range \$0–12,000), \$290 for co-payments (range \$0–9,000), \$110 for alternative treatments (range \$0–3741), and \$52 for counseling (range \$0–3000). Total mean direct cost per respondent per year was \$698. In the 7 days prior to completing the questionnaire, respondents reported a mean of 1.4 hours (of 36 hours) absent from work due to FD symptoms.

**Conclusion:** This is the first study to estimate direct and indirect costs of FD to patients. This study suggests that FD patients incur significant direct costs related to evaluating, testing and treating FD as well as indirect cost related to absenteeism and decreased productivity.

## 1057

**Functional Dyspepsia: The Patient's Perspective**

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**Purpose:** Functional dyspepsia (FD) is a highly prevalent disorder that significantly affects patients' quality of life. The aim of this study was to better understand the perspective of FD patients, with an emphasis on knowledge, fears and concerns.

**Methods:** ICD-9 codes identified adult patients ( $\geq 18$  years) with dyspepsia. Charts were individually reviewed to confirm the absence of organic disorders, to verify that patients met the Rome III criteria for FD, and to document a normal upper endoscopy. A questionnaire was mailed to patients meeting these criteria. Preliminary results obtained during the validation process (N = 47) demonstrated that the questionnaire is consistent, reliable and easy to use. (Kennedy et al, *Gastroenterology* 2007; 132: A68)

**Results:** 297 patients met all inclusion criteria and 60% (N = 179) responded. The mean age was 51  $\pm$  4 yrs, 75% were women, 90% were Caucasian, 49% had completed college, and 26% earned  $>$  \$50 k/yr. FD symptoms were present for 8  $\pm$  8 yrs and were rated as moderate (63%) or severe (22%). The most bothersome symptom was abdominal pain (35%), followed by abdominal burning (15%). Patients' most significant fears were that their symptoms would never go away (45%) and that FD could turn into cancer (20%). Only 33% of respondents recognized that FD is more common in women. A minority of respondents (26%) recognized that FD is more common than diabetes. 34% of patients believed that FD increased their risk of cancer, and 50% believed that FD increased their risk of ulcer disease. Respondents noted that FD may be caused by genetic factors (40%), dietary factors (70%), and anxiety or depression (68%). To diagnose FD, 55% stated that blood tests were needed, while 70% and 43% stated that EGD or ultrasound was required. Most felt that FD symptoms could be relieved by diet (77%) or medications (73%). Only 13% believed that FD symptoms could be improved by surgery.

**Conclusion:** This study confirms and extends our preliminary observations regarding patients' perspectives of FD. Patient misconceptions are common, despite the educational level of respondents. These misconceptions may contribute to the diminished quality of life seen in FD patients. Our results highlight the need to educate FD patients about their condition.

## 1058

**Impact of Combined Gastric and Sacral Stimulators on Upper/Lower Gastrointestinal and Urinary Symptoms**

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**Purpose:** Gastric Electrical Stimulation (GES) is available as a Humanitarian Use Device for patients with the symptoms of gastroparesis and is effective in reducing gastrointestinal symptoms. We have previously shown that patients with gastric motor disorders often have co-existing abnormalities of the genitourinary system (*Gastroenterol* 112: A737, 1997), which may now be treated with sacral electrical stimulation (SES), resulting in similar improvements in genitourinary symptoms. SES has been shown to be beneficial in controlling fecal incontinence and resistant idiopathic constipation.

**Methods:** We compared the results of therapy with GES and SES in 21 patients (19 F, 2 M, mean age of 39.7 years) who were implanted with both devices. Data for 16 patients is complete for upper and lower gastrointestinal and urinary symptoms. Patients had documented gastroparesis as well as bladder or other pelvic floor dysfunction. All 21 patients had received their GES before the SES. Patients were evaluated at baseline and latest follow up (median 4 years for GES and 2 years for SES). Scores of upper GI (GI: 0–4, TSS max 20), lower GI (GI: 0–3, TSS max 9 and BM's per day), and GU (GU: 0–3, UTSS, max 18) function were recorded. Results were compared by paired t-tests & reported as mean  $\pm$  SE.

**Results:** All 16 patients improved both upper and lower GI and GU symptoms. Improvement in all parameters as nausea (2.81 vs. 71), vomiting (3.98 vs. 1.69), anorexia (3.4 vs. 1.48), bloating (3.7 vs. 12.07), abdominal pain (3.8 vs. 1.48) and gastric total symptom score (TSS) (17.14 vs. 7.43), leakage (1.48 vs. 29), urinary urgency (1.62 vs. 62), voiding difficulty (2.0 vs. 52), straining (1.44 vs. 44), trouble starting stream (1.5 vs. 38), number of pads used (.62 vs. .1) and urinary total symptom score (UTSS) (8.69 vs. 2.69), fecal urgency (.89 vs. .58), constipation (2.15 vs. .74), fecal total symptom score (TSS) (3.63 vs. 1.63), and number of BM's per day (.97 vs. 1.7) were statistically significant. See table.

**Conclusion:** The combination of GES and SES appears to be both safe and effective for patients with con-comitant gastroparesis and bladder dysfunction and SES improved coexistent fecal abnormalities as well.

	Before GES/SES	After GES/SES	P values
Upper TSS	17.14	7.43	<0.01
Lower TSS	3.63	1.63	<0.01
Urinary TSS	8.69	2.69	<0.01

## 1059

**Can Thrombosis Be Predicted in Patients with Gastroparesis?**

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**Purpose:** Recent reports have shown that nearly 90% of patients with gastroparesis have some sort of detectable hypercoagulable state. Also, a recent series of gastroparesis patients has noted an unusually high incidence of deep venous thrombosis, pulmonary embolism and/or line related thrombosis. The purpose of our study was to retrospectively examine a group of patients with gastroparesis to identify risk factors for hypercoagulability.

**Methods:** We retrospectively examined a series of 191 patients (30 were male, 161 were female; 161 were white, 28 African American, and 2 were Hispanic with the average age of 44 years) with gastroparesis. We determined if these patients had history of DVT, PE and/or line-related thrombosis (CLOT, N = 50) or no history of thrombosis (NOCLLOT, N = 141).

Thirteen factors were compiled on these patients: activated Protein C resistance, fibrinogen levels, Protein C and S levels, antiphospholipid IgA, IgM and IgG levels, anti-b2-glycoprotein IgA, IgM, and IgG levels, Factor VIII levels, Antithrombin III levels, as well as the presence of the C677t methyl-tetrahydrofolate reductase mutation. We used Fisher's discriminant analysis to determine a linear function of these 13 variables that classified the 191 patients into either the CLOT or NOCLOT group. Because true clotting history was known, we were able to assess the ability of the function to classify each patient as if that patient's clotting status was unknown.

**Results:** Of our 191 patients, 50 of whom had history of abnormal clotting and 141 who did not, the derived function correctly classified 74% of the patients into either the CLOT or NOCLOT group. The classification was correct for 74% of the CLOT group (sensitivity) and 74% of the NOCLOT group (specificity).

**Conclusion:** Our results suggest that clotting risk can be accurately predicted with 74% certainty in these patients on the basis of his/her outcomes on the 13 factors listed above. Clinically, this could be used to risk stratify these patients, the majority of whom have some hypercoagulable propensity, for life-threatening thrombosis.

## 1060

### Does Maternal Predominance Exist in the Cyclic Vomiting Pattern in Gastroparesis?

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**Purpose:** A cyclic pattern of Gastroparesis has recently been described and shown to differ from non-cyclic patterns (NGM 18(8): A233, Aug 2006). Likewise, cyclic patterns have been associated with migraine, which is felt to be maternally inherited. We investigated the hypothesis that GP patients with a cyclic pattern might have a more maternal pattern of inheritance for migraine and related overlap syndromes.

**Methods:** From a data base of 345 consecutive patients seen, 48 patients (8 m, 40 f, mean age 41.5 yrs) with Diagnosis: 18 Idiopathic, 27 Diabetes Mellitus, 3 Post-Surgical disorders, presented with the symptoms (Sx) of GP. Most patients were drug refractory and referred for possible GES. Patients included 35 (3 m, 32 f) with Cyclic Symptoms (Cyc), and 13 (1 m, 12 f) with No Cyclic Symptoms (NoCyc). 38 of the 48 patients (25 Cyc and 13 NoCyc) underwent implantation of permanent GES, mean of 33 months. Family history of overlap syndromes and related disorders were determined by interview. Both Maternal and Paternal family histories were compiled for several overlap syndromes, as previously described (NGM, above).

**Results:** Maternal prevalence of migraine and related overlap syndromes was nearly universally higher in patients with cyclic symptoms (see table below) Vs those with non-cyclic symptoms.

**Conclusion:** GP patients with symptoms have a much higher female predominance of migraine and related overlap syndromes. These finding raise the possibility of genetic, possibly mitochondrial DNA-linked biologic component, in the cyclic nature of their symptoms.

	MHA	FMA	Anx/Dep	LDO	ANS	IBS	BLAD
Mat-CYC	0.45	0.09	0.59	0.05	0.36	0.18	0.36
Pat-CYC	0.09	0.05	0.18	0.09	0.14	0.09	0.09
P-value	0.006	0.003	0.005	0.56	0.85	0.39	0.03

## 1061

### Gastric Emptying Scintigraphy Results in the ROME III Subgroup Classifications for Functional Gastrointestinal Disorders

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**Purpose:** Delayed gastric emptying has been detected in 20 to 45% of patients with functional dyspepsia using gastric emptying scintigraphy (GES);

however, the association of symptoms to alterations in gastric emptying has been difficult to delineate. ROME III criteria classify functional dyspepsia by "meal-related" and "meal-unrelated" symptoms into *postprandial distress syndromes (PDS)* and *epigastric pain syndromes (EPS)*, respectively. Additionally, new categories of *chronic idiopathic nausea (CIN)* and *functional vomiting (FV)* have been recognized. Although these new classifications were devised to allow better pathophysiologic grouping for treatment purposes, the prevalence of abnormal gastric emptying in the Rome III subgroups has not been delineated.

**Aim:** The aim of this study was to compare GES results to Rome III symptom subgroup classifications.

**Methods:** We designed a retrospective analysis of consecutive patients undergoing GES at our tertiary care facility. GES was performed using 4 hour imaging after ingestion of a radiolabeled Eggbeaters sandwich. The PAGI-SYM questionnaire was completed at the time of imaging and used to classify patients into subgroups of FD, EPS, PDS, CIN, and FV. Subgroup classifications were then correlated to scintigraphy data.

**Results:** Of 99 consecutive patients undergoing GES from February 2007 to May 2007, 98 had analyzable GES data. GES revealed normal solid emptying in 58 patients, delayed solid emptying in 37, rapid emptying in 3. Of the 37 patients with delayed gastric emptying, fullness/bloating was described as the predominant symptom(s) in 15, vomiting in 9, abdominal pain/discomfort in 8, nausea in 7, reflux/heartburn in 7, regurgitation in 2, constipation in 2, and early satiety in 1. Classification by ROME III criteria revealed 61 patients with FD, 52 with PDS, 25 with EPS, 34 with CIN, and 27 with FV. Of these, delayed gastric emptying was seen in 25 of the 61 (41%) FD patients, 21 of the 52 (40%) with PDS, 11 of the 25 (44%) with EPS, 13 of 34 (38%) with CIN, and 14 of 27 (52%) with FV. Twenty-one patients were found to have no definable ROME III disorder; of these, fourteen had normal GES and seven with delayed.

**Conclusion:** In this tertiary care center experience, use of meal-related and meal-unrelated symptoms did not identify a group with delayed gastric emptying. There was a similar prevalence of delayed gastric emptying in the ROME III classifications of the functional gastroduodenal disorders.

## 1062

### Effects of Mesalazine Alone or Associated with Lactobacillus bouardii on Diarrhea-Predominant Irritable Bowel Syndrome

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**Purpose:** Recent studies have demonstrated that some irritable bowel syndrome (IBS) patients display persistent signs of minor mucosal inflammation<sup>1,2</sup>. Mesalazine (M) has intestinal anti-inflammatory properties<sup>3</sup> and probiotics may suppress the low-grade inflammation associated with IBS or restore normal local immune function<sup>4</sup>. The effects of M alone or combined therapy of M and probiotics on diarrhea-predominant IBS (IBS-d) is presently unknown.

**Aims:** Evaluate the effects of M and combined therapy of M with Lactobacillus bouardii (Lb) on symptoms of IBS-d patients.

**Methods:** Based on Rome III criteria, 34 IBS-d patients (18 year or more) were included. To exclude organic diseases all patients underwent colonoscopy, stool culture, serum anti-endomysium antibody, lactose tolerance test and parasitologic stool examination. Patients were divided in two groups: M Group (MG) -17 patients received M 800 mg t.i.d for 30 days and M Lb Group (MLbG) - 17 patients received M 800 mg t.i.d and Lb 200 mg t.i.d. for 30 days. Drugs that might have any effect on intestinal motility or secretion were not allowed. Symptom evaluation at baseline and after treatment were performed by means of a 4 point likert scale including: stool frequency, stool consistency (Bristol scale), abdominal pain and distension. Paired t test were used for statistical analyses.

**Results:** MG presented a statistically significant reduction of the total symptom ( $P < 0.0001$ ). The stool frequency significantly reduced ( $P < 0.0001$ ) and the stool consistency improved ( $P < 0.0001$ ). The abdominal pain ( $P < 0.0001$ ) and abdominal distention significantly reduced ( $P = 0.0002$ ). MLbG presented a statistically significant reduction of the total symptom ( $P < 0.0001$ ). Also, the stool frequency significantly reduced ( $P < 0.0001$ ) and the stool consistency improved ( $P < 0.0001$ ). The abdominal pain ( $P = 0.0003$ ) and abdominal distention significantly reduced ( $P = 0.0002$ ).

**Conclusion:** Use of M and combined therapy of M and Lb reduced key symptoms of IBS-d patients. These preliminary results warrant further larger studies. 1. Talley NJ *Lancet* 2002; 360:555–5642. 2. Spiller RC *Gut* 2000;47:804–8113. 3. MacDermott RP *Am J Gastroenterol* 2000; 95: 3343–3345. 4. Camilleri M *Journal of Clinical Gastroenterology*. 2006;40(3):264–269.

## 1063

### Familial Aggregation of Functional Dyspepsia: A Case-Control Study

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**Purpose:** Functional dyspepsia (FD) is common, impacts on quality of life and is very costly. The etiopathogenesis is uncertain. While in irritable bowel syndrome there is evidence that genetic and intra-familial factors may be involved, this has not been studied in FD. We hypothesized that if there is familial aggregation, there would be an increased frequency of FD in first-degree relatives of FD patients compared with relatives of controls (the patient's spouse).

**Methods:** The study design was a case-control study. Cases had undergone a negative esophagogastroduodenoscopy at the Mayo Clinic for assessment of dyspeptic symptoms; 455 were randomly selected from the endoscopy database using the relevant diagnostic codes. A self report bowel disease questionnaire (BDQ) that recorded symptoms, the somatic symptom checklist, and a family information form (FIF) to collect the names and addresses of all first-degree relatives were mailed to all cases and their spouses. A BDQ was then mailed to all first-degree relatives of study subjects identified from the FIF. FD diagnosis was based on the Rome II criteria.

**Results:** A total of 152 case-spouse pairs responded (33.4% of those mailed); 77 couples agreed to participate and gave family information. The BDQ was sent to a total of 261 eligible relatives; 180 (69%) returned complete questionnaires: 114 from case families, 66 from control families. A total of 37 cases reported FD and 21 of their 114 relatives reported FD (prevalence rate 18% [95% CI: 12%, 27%]). A total of 17 of the spouses reported FD and 4 of their 66 relatives had FD (prevalence rate 6% [95% CI: 2%, 15%]). (A chi-square test for the difference in proportions, 18% versus 6%,  $P = 0.03$ ). Based on the 22 matched sets of family relatives with completed questionnaires, 6 matched sets had a case family with one or more individuals reporting FD, but none of the matched control families had any individual report FD, while 3 matched sets had one or more of the control family members report FD and none of the individuals in the matched case families reported FD ( $P = 0.51$ , McNemar's test).

**Conclusion:** This study suggests familial aggregation of FD occurs, supporting a genetic or intra-familial environment component.

## 1064

### Satiety Testing: Effects of Nutrient and Water Loading on Gastric Volume and Emptying

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**Purpose:** Satiety tests to assess gastric accommodation in patients with functional dyspepsia are performed with either nutrient or water loading. Simultaneous gastric volume and emptying can be measured scintigraphically using gastric mucosal labeling with intravenous technetium-99m and gastric emptying of a meal labeled with indium-111. The aim of this study was to compare the results of satiety testing using nutrient and water loading on gastric volume and emptying.

**Methods:** Six normal subjects underwent satiety testing and simultaneous scintigraphic measurement of gastric volume and emptying: 3 with nutrient drink and 3 with water loading. During fasting, Tc-99m pertechnetate was injected IV to label the gastric mucosa followed by SPECT imaging to determine gastric volume. Subjects ingested either water or Ensure, labeled with indium-111 DTPA, until feeling completely full. SPECT imaging for gastric volume and anterior/posterior In-111 imaging for gastric emptying were performed over 4 hours.

**Results:** Subjects undergoing Ensure and water loading consumed similar amounts to achieve the sensation of fullness ( $1500 \pm 229$  ml and  $1500 \pm 87$  ml, respectively; mean  $\pm$  SEM). Gastric volume tended to be larger immediately after Ensure compared to water ( $1939 \pm 324$  and  $1395 \pm 294$  ml;  $P = 0.28$ ). At 60 min, postprandial gastric volume was significantly higher after Ensure ( $1789 \pm 203$  ml) than water ( $667 \pm 112$  ml;  $P = 0.008$ ). Higher gastric volume was persistent for the entire study period with Ensure. Gastric emptying of Ensure was delayed compared to water (gastric retention at 1 hour =  $85 \pm 3\%$  vs  $26 \pm 7\%$  for water;  $P = 0.0015$ ). Gastric volume in excess of estimated amount of liquid remaining (calculated by multiplying volume ingested with percent gastric retention) was significantly higher after Ensure ingestion than water (mean excess volume:  $543 \pm 16$  and  $175 \pm 107$  ml,  $P = 0.04$ ). This excess gastric volume represents gastric accommodation response and secretions.

**Conclusion:** Nutrient loading causes gastric accommodation which persists for at least 4 hours whereas water loading does not produce gastric accommodation. Although nutrient loading produces gastric accommodation response, it does not result in higher ingested volume than with water loading. This suggests maximum ingested volume during satiety testing is not a measure of gastric accommodation. Satiety tests in general should not be used as surrogate marker for gastric accommodation response.

## 1065

### Use of Telemedicine To Follow Symptoms and Disease Course in Patients with Gastroparesis: A Pilot Study

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**Purpose:** Chronic disease care, such as in gastroparesis, requires ongoing communication between patient and physician. Telemedicine eliminates geographic constraints and allows convenient access between patients and physicians. Remote patient monitoring through telemedicine has improved outcomes in disorders such as diabetes, heart failure and hypertension; but has not been used to any great extent in GI disorders. **Aims:** 1) To set up an operational Internet-based telemedicine system for convenient patient reporting of symptoms. 2) To evaluate the feasibility of monitoring symptoms of patients with gastroparesis.

**Methods:** In this pilot longitudinal study of patients with gastroparesis, a HIPAA compliant Internet-based telemedicine system was devised and used to follow patients' symptoms. Symptoms of gastroparesis were monitored using 9 symptoms modified from the Gastroparesis Cardinal Symptom Index (GCSI). Patients rated their symptoms – none, very mild, mild, moderate, severe, very severe. In addition, diabetic patients could report blood glucose levels. Selected patients were asked to participate and given a short instructional session on how to use the internet-based telemedicine system. They were asked to enter their symptoms on a frequent basis, at least 3 times a week.

**Results:** Ten patients with symptoms of gastroparesis were recruited to participate (9 idiopathic gastroparesis, 1 diabetic gastroparesis). During the

2-month monitoring period, 8 of the 10 patients reported their symptoms using this Internet-based telemedicine system. The number of days the patients entered their symptoms averaged  $18 \pm 16$  [mean  $\pm$  SD] with a range of 2 to 48 sessions per patient. Interestingly, some patients had stable symptoms, whereas other patients had periods of symptom exacerbations. Increases in symptom scores were seen prior to patient visits to emergency rooms and hospitalizations. In addition, decreases in symptom scores were seen with instituting new treatments in some patients.

**Conclusion:** This pilot study shows that an Internet-based telemedicine system can be used to follow patients' symptoms. Use of telemedicine may be useful to follow individual patient symptoms – both monitoring for symptom exacerbations and symptom response to treatments. This discrete data compiled on a regular basis over a long period provides a unique insight into the disease course of patients with gastroparesis.

## 1066

### Clinical Characteristics, Diagnostic Features, and Response to Therapy in Patients with Rumination Syndrome

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**Purpose:** The aim of this study was to retrospectively investigate the demographics, clinical features, and response to therapy in patients meeting the Rome III criteria for rumination syndrome.

**Methods:** Retrospective chart review for the diagnosis of rumination syndrome in patients treated at the University of Kansas was performed. Patients were then contacted via mailed questionnaire and/or telephone interview. Data gathered included timing of episodes of emesis, additional symptomatology, gastric emptying results (using a 4 hour study with a 2% egg beaters<sup>®</sup> meal; normal retention  $N = <10\%$  @ 4 hours), the use of behavioral therapy and/or tricyclic antidepressants, and subjective and objective markers for overall patient improvement.

**Results:** Thirty-six newly-diagnosed patients with rumination syndrome (range = 14–67 y/o; mean  $N = 32.2$  y/o) were identified from 2000–2007. Each had failed prior therapy with traditional anti-emetic and prokinetic agents initially prescribed for alternate diagnoses; none met criteria for an underlying eating disorder (i.e. bulimia nervosa). Nausea was present in over 90% of patients but did not always precede their bouts of emesis. The timing of the vomiting was directly related to eating, with most patients reporting episodes of effortless vomiting within 15 minutes of the onset of meals, including liquids. Both abdominal pain (epigastric pressure and fullness) and weight loss were co-morbid factors (80–90%), with weight loss attributed in part to avoidance of food in social settings. Of note, 19% of the patients (7/36) had evidence of underlying delayed gastric emptying while the remainder (29/36; 81%) were normal. Patients were treated with behavioral therapy (relaxation tapes, breathing exercises, etc.) and/or tricyclic antidepressants for pain modification. The average symptom reduction achieved was approximately 20–50% (range 0–100%), with the time to improvement routinely reported as 2–8 weeks following the initiation of therapy.

**Conclusion:** Rumination syndrome: 1) is an under-recognized entity in gastroenterology practice, 2) can present with normal or slow gastric emptying, and 3) characteristically presents with effortless vomiting immediately following ingestion of meals. Behavioral therapy is the primary treatment for this disorder and often results in symptomatic and quality of life improvements.

## 1067

### Double Blinded Randomized Study of Temporary Gastric Electrical Stimulation (GES): Preliminary Results of EndoSTIM Study and Correlation with Mucosal EGG

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**Purpose:** We recently reported on temporary GES (TGES) in a double blinded manner (DDW abstract 2007). We have also reported that the endoscopic mucosal EGG, done at the time of temporary electrode placement, may predict response to TGES therapy (ACG abstract 2006).

**Methods:** We studied 58 patients (11 males, 47 females, mean age 46 years) with the symptoms of gastroparesis (GP) and underlying diagnosis: (Idiopathic (ID),  $N = 38$ ; Diabetes Mellitus (DM),  $N = 13$ ; Post-surgical (PS),  $N = 7$ ) in a randomized placebo-controlled cross over study of TGES as two consecutive four day sessions. We compared via linear regression the baseline factors that correlated with the outcome of reduction in vomiting. We examined all baseline characteristics, including symptoms and physiologic measures versus outcome of vomiting, when the device was randomized to ON or OFF.

**Results:** 28 patients had ON-OFF and 30 patients had OFF-ON; 45 of 58 patients finished all 8 days. When analyzed for all patients ON versus all patients OFF both vomiting frequency and HRQOL improved significantly ( $P < 0.05$ ). By linear regression, a number of baseline parameters correlated with outcome of TGES. Endoscopic mucosal EGG correlated greater with outcome than did cutaneous EGG (See table 1).

**Conclusion:** TGES has now been shown effective by evidence based criteria. A number of baseline characteristics correlate with the outcome of TGES. The correlation of mucosal EGG may be particularly important, as this measure can be done endoscopically at the time of temporary electrode placement.

Table 1. Linear Regression Model Predictive Factors at Day 4

Measure	Vomiting Correlation	Nausea Correlation	TSS Correlation
Device ON or OFF	$P = 0.01$		
Baseline TSS	$P = 0.04$		$P = 0.06$
Baseline GET 1 hour	$P = 0.02$	$P = 0.04$	$P = 0.03$
Cyclic or non-cyclic sx pattern	$P = 0.02$		
Mucosal EGG at TGES placement	$P = 0.05$		
Baseline EGG average frequency	$P = 0.16$		$P = 0.09$

## 1068

### Rifaximin Therapy for Rome II-Positive Irritable Bowel Syndrome (IBS)

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**Purpose:** An emerging hypothesis suggests that small intestinal bacterial overgrowth (SIBO) may contribute to IBS pathophysiology. Rifaximin is a nonabsorbable antibiotic with broad-spectrum activity against intestinal pathogens. Studies have demonstrated that reduction of SIBO with rifaximin may improve IBS symptoms. This retrospective chart review evaluated rifaximin, administered alone or with other therapies, in improving functional gastrointestinal (GI) symptoms in IBS patients.

**Methods:** Consecutive adult patients meeting Rome II criteria for IBS with no history of IBD or bowel resection surgery were identified. Patients received rifaximin 400 mg two or three times daily for 10 days. Most patients reporting partial relief of GI symptoms, or return of symptoms after completing rifaximin treatment, received  $\geq 1$  additional rifaximin regimen. Concomitant medications were permitted. Study endpoint was percentage of patients reporting complete or partial relief of baseline functional GI symptoms following rifaximin treatment.

**Results:** Analysis included 104 patients (mean age, 49.3 y) with mean IBS duration of 3.8 y (range, 0–30 y). Forty patients (38%) had diarrhea-predominant IBS (IBS-D), 23 (22%) had constipation-predominant IBS (IBS-C), and 27 (26%) had alternating-form IBS (IBS-A). The most

frequently reported baseline IBS symptoms were diarrhea (26%), constipation (15%), bloating (13%), abdominal pain (10%), and gas (7%). Initially, 80 patients (77%) received rifaximin 800 mg/d and 24 patients (23%) received rifaximin 1200 mg/d for 10 days. Thirty-five patients (34%) received >1 rifaximin regimen. Concomitant GI medications during rifaximin therapy included tegaserod (11%), hyoscyamine (6%), rabeprazole (4%), loperamide (3%), chlorthalidone/clidinium (3%), dicyclomine (2%), belladonna (<1%), oxybutynin (<1%), doxycycline (<1%), and fiber (<1%). Thirty-four patients (33%) reported complete relief and 71 patients (68%) reported partial or complete relief of baseline IBS symptoms following  $\geq 1$  rifaximin regimen. Symptom improvement was associated with IBS subtype, with 40% of IBS-D patients, and only 13% of IBS-C patients, reporting complete relief of baseline IBS symptoms following rifaximin treatment. Adverse events associated with rifaximin were mild.

**Conclusion:** In this chart review, rifaximin 800 to 1200 mg/d for 10 days improved functional GI symptoms in patients with Rome II IBS. These findings provide additional evidence of the benefits of rifaximin, administered alone or with other therapies, for IBS patients. Controlled trials are warranted to further evaluate these findings.

## 1069

### Functional Gastrointestinal Disorder Comorbidities: Comparisons of Prevalence and Costs in the 6 Months before and after Diagnoses of Constipation (C) and Irritable Bowel Syndrome and Constipation (IBS+C)

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**Purpose:** Patients with C and IBS can present with a wide range of functional gastrointestinal disorder (FGID) comorbidities. However, it is unknown how often these comorbidities occur or their temporal relationship to C and IBS. Few studies have differentiated the occurrence of FGID comorbidities before and after diagnoses of C and IBS.

**Objective:** To evaluate the prevalence and costs of FGID comorbidities in a large sample of patients in the 6 months before and after diagnoses (DXs) of C and IBS+C (co-occurring DXs of IBS and C).

**Methods:** A retrospective analysis was performed in an employer database of greater than 500,000 employees. Patient cohorts with C (ICD9s 564.0, 564.00, 564.01, and 564.09), IBS+C (ICD9 564.1  $\times$  and co-occurring C) and a Control group (neither C nor IBS+C) were identified. For each IBS+C patient identified, 5 C patients and 180 Control patients were matched using logistic regression and propensity scores for age, job tenure, gender, marital status, race, exempt- and full-time employment status, salary, region, Charlson Comorbidity Index Score, and the existence of medical claims. Prevalence and costs for FGID co-morbidities were calculated for the 6 months before and after C and IBS+C DXs by FGID ICD9 code (see figure). Comorbidity comparisons were performed within (before vs after) and between

Diagnosis (ICD9)	Time (relative to DX)	Prevalence (% of cohort)		6-Month Costs	
		C	IBS+C	C	IBS+C
Hemorrhoids (455.xx)	Before	4.14 <sup>†</sup>	8.09 <sup>†</sup>	\$15.9 <sup>†</sup>	\$28.4 <sup>†</sup>
	After	12.49 <sup>§</sup>	17.80 <sup>§</sup>	\$46.4 <sup>§</sup>	\$82.7 <sup>§*</sup>
Intestinal Obstruction (560.xx)	Before	0.78 <sup>†</sup>	2.59 <sup>†</sup>	\$15.5	\$69.8
	After	1.49 <sup>†</sup>	2.91 <sup>†</sup>	\$21.6	\$23.2
Anal Fissure (565.0x)	Before	0.52 <sup>†</sup>	0.32	\$2.5	\$14.5
	After	1.17 <sup>†*</sup>	1.62 <sup>†*</sup>	\$9.0 <sup>†</sup>	\$8.3
Impaction of Intestine (560.3x)	Before	0.19 <sup>†</sup>	0.65 <sup>†</sup>	\$0.3	\$0.7
	After	0.26 <sup>†*</sup>	1.62 <sup>†</sup>	\$0.5	\$1.6
Ulcer of Anus and Rectum (569.41)	Before	0.00	0.65 <sup>†</sup>	\$0.0	\$0.0
	After	0.19 <sup>†</sup>	0.00	\$1.4	\$0.0

Between-group comparisons: †  $P \leq 0.01$  (vs Control); ‡  $P \leq 0.01$  (IBS-C vs C); Within-group comparisons (Before- vs After-DX): §  $P \leq 0.01$ ; \*  $P \leq 0.05$

(C vs IBS-C vs control) groups. Prevalence comparisons used z-scores of log odds ratios (Woolf method) and costs were compared by Satterthwaite t-tests.

**Results:** Data were available for 309 IBS-C patients, 1545 C patients, and 55,620 matched Controls. All cohorts averaged 41 years of age and 74% were female. The prevalence and costs of FGID comorbidities within and between C, IBS-C, and Control groups generally increased. Many findings were significant (see figure).[figure1]

**Conclusion:** The prevalence and costs of FGID comorbidities increase after diagnoses of C and IBS+C. Prevalence and costs of comorbidities were similar between C and IBS+C cohorts.

## 1070

### Type D Personality Is Associated with Impaired Health-Related Quality of Life in Patients with Functional Bowel Disorders (FBDs)

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**Purpose:** Few data are available on the impact of personality traits on HRQoL in FBDs. Type D personality is characterized by a tendency to experience negative emotions and to inhibit these emotions while avoiding social contacts with others. We evaluated the hypothesis that Type D personality would be associated with impaired HRQoL in FBDs.

**Methods:** Data were collected from consecutive patients undergoing hydrogen breath testing for functional GI symptoms at a tertiary clinic. They completed the Type D Scale – 14 and the Short-Form Health Survey 12 (SF-12v2) questionnaires. Standardized cut-offs  $\geq 10$  identified Type-D caseness. Discrete variables were compared with chi-square test. Continuous variables were compared with Student's *t* test. Differences between personality types on HRQoL were analyzed using MANOVA. Multivariable logistic regression analyses were used to examine if Type D was an independent determinant of impaired HRQoL.

**Results:** Of 122 patients, 37% met criteria for Type D personality. Groups did not differ in age ( $61 \pm 15$  vs  $59 \pm 18$  yrs) or gender (72% F). Type D patients had significantly lower scores on the Physical Component scale (PCS) and the Mental Component scale (MCS) of the SF-12 and all SF-12 subscales compared with non-Type D patients. Type D personality remained an independent predictor of impaired PCS and MCS after adjusting for demographic and clinical characteristics.

#### Type D personality and impaired HRQoL

	OR	95% CI	P-Value
<i>SF-12 component scores</i>			
PCS	4.13	1.78–9.80	0.001
MCS	11.03	3.25–37.49	0.000
<i>SF-12 subscales</i>			
Physical Function	5.16	1.97–13.56	0.001
Role Physical	5.98	2.41–14.85	0.001
Bodily Pain	4.36	1.72–11.08	0.002
General Health	4.96	1.57–15.71	0.006
Vitality	7.21	2.54–20.44	0.000
Social Function	9.12	1.75–47.63	0.009
Role Emotional	19.05	4.61–52.06	0.000
Mental Health	15.49	4.61–52.06	0.000

**Conclusion:** Type D personality was associated with an increased risk of impaired HRQoL in FBD patients. Type D personality construct may be an important consideration when assessing HRQoL outcomes. Consideration of personality type could improve risk stratification in research and clinical practice in this patient group.

1071

### Prevalence of Functional GI Disorders in Women with History of Domestic Violence. Does the Type of Abuse Matter?

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**Purpose:** Previous studies have documented a high prevalence of abuse, either physical or sexual, in patients with functional gastrointestinal disorders (FGIDs). However, there is a lack of information regarding prevalence of FGIDs in adults suffering domestic violence. Our aim was to evaluate the prevalence of FGIDs in women with domestic violence and explore if the type of abuse has any relationship with the presence of FGIDs.

**Methods:** 122 women at "Casa de la Mujer", a Women's Attention Center that gives support to women who experience domestic violence, were invited to participate. Prevalence of FGIDs was assessed using the Rome II integrated questionnaire (Spanish validated version). Physical, psychological and sexual abuse were assessed using a standard self reporting screening instrument, and anxiety-depression levels using the Hospital Anxiety and Depression scale (HAD) questionnaire.

**Results:** 87 (71%) women (mean age  $39 \pm 11$  years) agreed to participate in the study. 85(98%) reported psychological abuse, 66 (76%) physical, and 26 (30%) sexual abuse. Prevalence of FGIDs was 93% (N = 81) and 71 women had more than 1 FGID (mean  $3 \pm 1$ ). FGIDs reported were: functional dyspepsia 59%, IBS 39%, proctalgia fugax 38%, functional constipation 31%, functional heartburn 22%, bloating 18%, fecal incontinence 13%, dyssynergia fecation 9%, abdominal pain 8%, chest pain 8%, rumination 5%, and dysphagia 2%. 25 women had both dyspepsia and IBS. The mean global score for HAD was  $19 \pm 7$ . Women with FGIDs had significantly higher anxiety scores ( $11 \pm 4$  vs  $6 \pm 1$ ,  $P = 0.005$ ). Fecal incontinence ( $P = 0.05$ ) and proctalgia fugax ( $P = 0.04$ ) were more common in women with sexual abuse compared to other types of abuse. Women with sexual abuse had higher global and anxiety scores (HAD) ( $P < 0.05$ ).

**Conclusion:** Most women who suffer domestic violence experience FGIDs, confirming that abuse plays an important role in FGIDs. Psychological distress, specifically anxiety, was more severe in women with FGIDs. Sexual abuse is associated with functional anorectal disorders. We believe our study has important clinical implications for comprehensive health care of women in situations of abuse and women with FGIDs.

1072

### Pilot Study on Patient Centered Educational Intervention in Irritable Bowel Syndrome (IBS)

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**Purpose:** We tested the effectiveness of an individualized theory based educational intervention on a) IBS quality of life (IBS-QOL) and b) health cognition (CG-FBD).

**Methods:** Subjects with IBS were randomized into an education- (E) group, who received a 30 min individualized educational intervention based on Knowles' theory of adult learning, or control group (C)- who read about IBS for 30 min. Outcomes were measured at 1 and 3 months post intervention. Analyses were done using a repeated measures ANOVA model. The regression parameter of interest was group modification of the change in outcome measures from baseline to follow-up.

**Results:** 50 subjects (1:1) were enrolled. Baseline differences in the E vs. C group were noted for IBS-QOL (scale 0–100);  $P = 0.01$ , and for disease-related cognition (CG-FBD) (scale 1–7, 7 = poorest cognition);  $P = 0.0002$ . Accordingly, adjustments were made. In the adjusted analysis, there were notable observations about the E vs. C group (Table 1): 1) IBS-QOL improved in the E group between baseline to 3 months ( $P = 0.003$ ) and between 1–3 months ( $P = 0.03$ ). Although these changes were statistically significant, they did not reach clinical relevancy; 2) A trend towards improvement in CG-FBD was noted in the E group from 0–1 month ( $P = 0.06$ ) and 0–1–3 months ( $P = 0.10$ ). At 0–3 and 1–3 months, changes were not statistically significant ( $P = 0.24$  and  $P = 0.79$  correspondingly). A change of 0.5 on a 1–7 scale is clinically significant; and 3) A trend of improvement of perceived control over the illness was noted in the E group.

**Conclusion:** The study provides preliminary data that our educational model has the potential to improve disease-related cognition, IBS-QOL, and perceived control over the illness. The intervention is practical, inexpensive and can be provided by a health care provider trained in the model.

1073

### Rifaximin and IBS in the Adolescent Patients

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**Purpose:** To evaluate the efficacy of Rifaximin in the adolescent patients with IBS. Irritable bowel syndrome (IBS) is a frequently encountered problem affecting the adolescent population. Medical help is only sought when IBS starts to affects their school performance as well as social lifestyle. Delay in seeking medical help is most likely due to embarrassing symptoms. Adolescent patients with IBS presents with bloating, abdominal cramps, and extreme urgency to defecate, fear of soiling, uncontrollable flatulence, diarrhea and sometimes constipation. Etiology of IBS is not clearly understood or established but inflammation, infectious gastroenteritis, small bowel bacterial overgrowth, visceral hypersensitivity and altered gastrointestinal motility have been suggested as interrelated in pathophysiology of IBS. Multiple therapeutic options including probiotics, fiber, laxatives, stool softeners, antispasmodics and antidarrheals are available but not much success has been documented with these treatments. Mostly these patients take various combinations of prescription as well as over the counter medications without much relief.

**Methods:** We evaluated 29 patients (age 15 to 19 years, 20 females and 9 males) who were diagnosed with IBS and were already on different treatments without any success for a long period of time. After initial evaluation, these patients were started on Rifaximin 400 mg twice a day for a period

IBS-QOL and CG-FBD Scores

		Group					
		Education (N = 25)			Control (N = 25)		
		Baseline	1-Month	3-Month	Baseline	1-Month	3-Month
Outcomes	IBS-QOL	$64.5 \pm 27.7$	$65.3 \pm 25.4$	$68.1 \pm 26.4$	$82.0 \pm 18.0$	$87.5 \pm 21.4$	$81.2 \pm 25.9$
	CG-FBD	$4.8 \pm 1.2$	$4.5 \pm 1.2$	$4.4 \pm 1.2$	$3.6 \pm 1.1$	$3.6 \pm 1.2$	$3.7 \pm 1.4$

of 10 days to one month. Two patients required a second course after one month of initial treatment due to recurrence of symptoms.

**Results:** After the treatment, 24 patients improved significantly with almost complete resolution of their symptoms, two subjects required a second course of treatment and three patients continued with IBS symptoms. Their quality of life as well as school performance and attendance improved significantly. They were not fearful of using the subway or school buses.

**Conclusion:** Among other treatment options available for IBS, Rifaximin appears to be well tolerated and efficacious as the first line of therapy for the adolescent population.

## 1074

### Prevalence and Predictors of Non-Consulting for Chronic Constipation

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**Purpose:** It is unknown what proportion of U.S. health maintenance organization (HMO) subscribers have chronic constipation but do not consult health care providers about this problem. This work evaluated the prevalence and predictors of non-consulting constipation, and the quality of life (QoL) and psychological symptoms in these individuals.

**Methods:** Adults enrolled in a large West Coast U.S. HMO with one or more constipation visits on record in the past year, and a comparison sample matched for age and gender with no constipation-related visits in the past 5 years, completed a mail survey including demographics, Rome III IBS and constipation modules, PAC-QOL and SF-12 QoL questionnaires, and the Brief Symptom Inventory-18.

**Results:** 671 constipation consulters (mean age 66.1 years, 68.5% female) and 1022 comparison subjects (mean age 66.4 years, 68.0% female) completed the survey (60% overall response). 77.5% of the consulting sample and 40.5% of the comparison sample met Rome III Chronic Constipation (CC) criteria. CC non-consulters did not differ from CC consulters in age, gender, race, psychological symptoms or SF-12 mental composite scores. However, compared to CC-consulters, the CC-non-consulters had higher SF-12 physical composite QoL scores (Mean  $\pm$  S.D: 43.3  $\pm$  13.2 vs. 39.6  $\pm$  13.3;  $P < .0001$ ), and less constipation-related QoL impairment on the PAC-QOL (36.0  $\pm$  19.0 vs. 46.6  $\pm$  19.6;  $P < .0001$ ), less frequent abdominal pain and bloating ( $P < .0001$  for both), and were less likely to meet Rome III IBS criteria (43.2% vs. 58.7%;  $P < .0001$ ). Compared to survey respondents without bowel problems (no Rome III IBS or CC) in the comparison sample, CC non-consulters had lower SF-12 physical (43.3  $\pm$  13.2 vs. 46.3  $\pm$  11.6;  $P < .0001$ ), and mental (50.1  $\pm$  10.5 vs. 54.2  $\pm$  8.3;  $P < .0001$ ) composite scores, as well as higher ( $P < .0001$ ) BSI-18 anxiety, depression, somatization and general distress scores.

**Conclusion:** Four out of 10 adult HMO patients have CC without consulting health care providers about it. Our data indicate that whether patients consult doctors about CC is unrelated to demographic or psychological characteristics, but related to constipation frequency, amount of associated abdominal pain and bloating, and impact on life functioning. CC non-consulters have significantly poorer QoL and more psychological symptoms compared to individuals without bowel problems. [Supported by Novartis Pharmaceuticals and R24 DK69674].

## 1075

### Investigation of Wireless Capsule (SmartPill®) for Colonic Transit: A Comparative Study with Radiopaque Markers in Health and Constipation

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**Purpose:** Traditionally, colonic transit time (CTT) has been assessed with radiopaque marker (Sitzmarks® (SZ)) technique. Although useful, it requires radiation and is hindered by poor patient compliance and complex protocols. This multicenter study aimed to simultaneously assess and compare CTT as measured by SmartPill® (SP)-wireless pH and pressure recording capsule with that of Sitzmarks® in constipated (Rome II) and healthy subjects.

**Methods:** After overnight fast, subjects ingested a nutrient bar (260 kcal) followed by a Sitzmarks® (24 markers) and a SmartPill® capsule. Subjects wore a data receiver for 5 days or until SmartPill® was expelled and kept stool diary. Abdominal x-rays were obtained on days 2 & 5. SmartPill® tracing was examined to assess gastric emptying time (GET) (time to rise in pH>4), small bowel transit time (SBTT) (time to cecal entry with >1 pH drop after GET), CTT (time from cecal entry to abrupt temperature drop), and whole gut transit time (WGTT). To account for the known influence of gender and age on CTT, analysis of covariance was used in the statistical examination of SmartPill® CTT.

**Results:** Table (mean  $\pm$  SEM, \* =  $P < 0.05$ ). 71 constipated (m/f = 8/63) and 83 healthy (m/f = 42/41) subjects participated. CTT, WGTT, day 2 Sitzmarks® transit, and day 5 Sitzmarks® transit were different ( $P < 0.001$ ) between constipated patients and controls, even after accounting for gender and age. CTT correlations between SmartPill® and % of markers expelled on day 5 were  $r = 0.59$  ( $P < 0.0001$ ) in patients and  $r = 0.46$  ( $P < 0.001$ ) in controls. The diagnostic utility of CTT to predict historical diagnosis of constipation was satisfactory with a computed ROC AUC of 0.74. Patients had slower ( $P < 0.001$ ) GET, slower ( $P < 0.01$ ) CTT, and slower ( $P < 0.02$ ) WGTT compared to controls. There were no serious adverse events.

**Conclusion:** SmartPill® is a novel, and more useful technique of assessing CTT. Its transit highly correlates with Sitzmarks®, and it provides comparable data. Additionally, it provides regional information on GET and SBTT. Thus, SmartPill® provides comprehensive data under physiological conditions, on whole gut and regional transit time in health and functional GI disorders.

## 1076

### Prevalence and Risk Factors for Abdominal Bloating and Visible Distention: A Population-Based Cross Sectional Survey

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**Purpose:** Abdominal bloating and visible distention are common yet poorly understood symptoms. Whether the characteristics of those with visible distention differ from bloating without distention is unknown. We aimed to

	GET	SBTT	CTT	WGTT	# Markers Day 2	# Markers Day 5
Controls	3.6 $\pm$ 0.2	3.8 $\pm$ 0.1	29.8 $\pm$ 2.7	37.2 $\pm$ 2.7	8.8 $\pm$ 0.9	1.2 $\pm$ 0.4
Constipated	5.7 $\pm$ 1.2*	4.4 $\pm$ 0.2	59.3 $\pm$ 4.5*	68.3 $\pm$ 4.3*	16.1 $\pm$ 1.0	6.9 $\pm$ 1.0*



evaluate in a representative US population the prevalence of bloating and distention, potential risk factors, and the distribution of functional GI disorders (FGIDs).

**Methods:** A symptom questionnaire was mailed to a previously assembled cohort that had been selected at random from the population of Olmsted County, MN. The complete medical records were abstracted. This questionnaire measured abdominal bloating and separately visible distention.

**Results:** Among the 2259 subjects (53% female; mean age 62 yrs), 615 reported bloating (272 with and 343 without visible distention). The sex-specific, age-adjusted (US White 2000) prevalence for bloating was 18.8% (CI: 16.6, 20.9) and for visible distention 8.9% (CI: 7.2, 10.6). Female gender, higher somatic symptom score, irritable bowel syndrome (IBS), functional dyspepsia (FD) and gastroesophageal reflux disease (GERD) were risk factors for bloating as well as for visible distention (Table). Further, female gender, higher somatic symptom score, IBS and specifically, IBS-constipation (IBS-C) and IBS-mixed (IBS-M), FD but not GERD significantly increased the odds for distention compared to bloating alone (Table).

**Conclusion:** Bloating and visible distention are common in the community, and have similar risk factors. Female gender, somatic symptom score, IBS-C, IBS-M, and FD increased the risk for distention versus bloating alone.

**Table:** Risk factors for bloating and distention

	OR for bloating	OR for distention	OR for distention vs bloating
Female vs male	1.9 (1.5, 2.4)	2.7 (2.1, 3.6)	1.5 (1.0, 2.1)
SSC score per 1 unit	3.6 (2.9, 4.6)	5.2 (4.1, 6.6)	1.4 (1.1, 1.8)
IBS vs no IBS	4.0 (2.8, 5.8)	7.4 (5.1, 10.7)	1.9 (1.3, 2.7)
IBS-C vs no IBS	4.5 (2.4, 8.5)	11.9 (6.6, 21.7)	2.7 (1.5, 4.8)
IBS-M vs no IBS	12.4 (3.9, 38.8)	26.8 (8.8, 82.2)	2.2 (1.1, 4.4)
FD vs no FD	2.9 (1.7, 5.0)	6.3 (3.8, 10.5)	2.2 (1.3, 3.7)
GERD vs no GERD	2.7 (2.0, 3.6)	3.2 (2.3, 4.4)	1.2 (0.9, 1.7)

## 1077

### Studies of the Efficacy of Gastric Electrical Stimulation for Gastroparesis-US/European Comparison—2007

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**Purpose:** Gastric Electrical Stimulation (GES) is an accepted therapy for drug refractory gastroparesis (GP). However, reports of efficacy have varied between centers. We aimed to compare results from several centers for the efficacy of GES by standardizing data between centers\*.

**Methods:** Consecutive patients with the symptoms of gastroparesis were evaluated at each center located in Western Europe (4 centers) and Southern US (4 centers). The patients were by demographics (sex; age), underlying diagnosis (Idiopathic GP = I, Diabetic GP = D, Postsurgical GP = P), % of centers where GET criteria were used, months (Mos) since implant, percentage change in symptoms (baseline to latest for Vomiting = Vom and GI Total Symptom Score = TSS).

**Results:** See Table. The European centers show a higher percentage change in vomiting than the US centers. However, the European centres had a larger proportion of DGP patients compared to US centres (59% vs 22%) and a smaller proportion of IGP patients (25% vs 72%).

**Conclusion:** This is the first non-formal trial comparison of the use of GES for patients with the Symptoms of Gastroparesis confirming effectiveness of GES. The specific localities studied (both US & Europe) reveal similarities but also differences between centers, particularly with respect to DGP/IGP proportions. Ongoing prospective comparisons of outcome data are feasible and may be warranted with the continued clinical use of GES.

Locat	No	F, M; yr	DX:I, D, P	GET	Mos	Vom	TSS
EUR	61	38,23;41	15,36,10	100%	35	62.0	48.0 (one centre)
US	319	258,61;42	231,71,17	75%	49	45.0	38.0
ALL	380	296,84;42	246,107,27	88%	47	48.0	38.5

\*EXACTS (European Across American Comparative Trial of Stimulation) is formed by ASSESS (Associated Southern Sites of Electrical Stimulation Studies) and EDGES (European Data of Gastric Electrical Stimulation).

## 1078

### Complete Spontaneous Bowel Movement Frequency as Primary Outcome Measure in Patients with Chronic Constipation Treated with Linacotide

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**Purpose:** Complete spontaneous bowel movement (CSBM) is an attractive symptom-specific primary endpoint for trials of patients with chronic constipation (CC), as it integrates the objective, quantitative sign of stool frequency and the subjective, qualitative symptom of sensation of complete defecation. Data from Phase 1 and 2 studies of linacotide, a first-in-class agonist of guanylate cyclase-C, were evaluated to compare attributes of CSBM with SBM as the primary outcome measure.

**Methods:** Two studies of oral linacotide, a Phase 1 study in healthy volunteers (HVs) and a multicenter Phase 2 study in patients with CC, evaluated bowel habits of stool frequency, stool consistency, straining, and sensation of complete evacuation. The CC study also evaluated global assessments of abdominal discomfort, severity of constipation, and relief of symptoms. Treatment effects of linacotide doses were compared with placebo using ANCOVA and Pearson's correlation coefficients of outcome measures were derived.

**Results:** Data from 48 HVs and 36 CC patients were analyzed. The mean weekly baseline SBM and CSBM rates were 6.4 and 5.8 among HVs, and 1.9 and 0.23 among CCs. In HVs, the mean baseline CSBM:SBM ratio was 0.89 and was essentially unaffected by linacotide treatment. In CC patients, the mean CSBM:SBM ratio was 0.11 at baseline and progressively increased with increasing dose of linacotide (0.29 in placebo to 0.45 at high dose). In CC patients, a comparison of CSBM and SBM responder analyses indicated that CSBM is more specific (11% vs 44% placebo response and a treatment effect of ~4-fold vs ~2-fold increase over placebo, respectively) but less sensitive (43% vs 100% maximum response, respectively). In addition, CSBMs were more strongly correlated than SBMs with other bowel habits ( $r = 0.70-0.72$  vs  $0.42-0.47$ ) and global assessments ( $|r| = 0.58-0.71$  vs  $0.42-0.49$ ).

**Conclusion:** These data indicate that the normal rate of CSBMs in HVs is approximately 1 per day, essentially the same as the rate of SBMs. CC patients have both a lower frequency of CSBMs and SBMs, and a lower ratio of CSBM:SBM compared with HVs. This ratio increased in CC patients in parallel with response to treatment. CSBM compared to SBM demonstrated a lower placebo response and a higher treatment effect relative to placebo and correlated more strongly with other bowel habits and global assessments. Based on these results, CSBM may be the preferred symptom-specific primary endpoint for clinical trials of new treatments for CC.

## 1079

### Does Testing for Markers of Inflammation Assist in Differentiating IBS from Other Organic Diseases?

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**Purpose:** Many clinicians remain uncomfortable making an IBS diagnosis based on symptom criteria and an absence of warning features. A biologic marker would have potential value in excluding other organic diseases. Markers of inflammation such as c-reactive protein (CRP) and fecal lactoferrin and calprotectin have been proposed as potentially useful in this regard. This study aims to assess the clinical usefulness of CRP, lactoferrin and calprotectin in differentiating IBS from other organic diseases.

**Methods:** This is an ongoing, prospective study. A consecutive sample of patients with abdominal pain, diarrhea and/or constipation referred for consultation in a tertiary care setting were offered enrollment. Patients were excluded if they had a known diagnosis of inflammatory bowel disease, prior GI resection, cancer or weight loss > 10 lbs within 6 months. All patients were requested to complete a validated bowel disease questionnaire and have CBC, albumin, TTG Ab, CRP, TSH, stool lactoferrin and calprotectin tests performed. Colonoscopy and other testing was performed if deemed clinically appropriate. The medical record was reviewed to determine clinical diagnosis and fulfillment of Rome III criteria. Data were analyzed using Chi-square analysis to assess associations between IBS diagnosis (clinical and Rome III) or other functional bowel disorder versus other organic disease and these markers.

**Results:** 26 patients have been enrolled to date (female = 20, male = 6; age range 19 – 67 years [mean 36 yrs]). Diagnosis at last follow-up (N = 26): IBS-D 14, IBS-C 4, IBS-A 1, chronic constipation 2, dyssynergic defecation 1, Crohn's disease 1, small bowel bacterial overgrowth 2, no diagnosis recorded 1. Abnormal test results at initial evaluation: hemoglobin < 12.0 in 3, albumin < 3.5 in 2, abnormal colonoscopy in 2, CRP positive in 2, lactoferrin positive in 2, calprotectin positive in 7. No patient had positive celiac antibodies. Chi square values were not significant for an association between IBS vs. non-functional diagnosis and CRP, lactoferrin, calprotectin or any positive single test.

**Conclusion:** Results from this interim analysis do not support routinely checking CRP, fecal calprotectin and lactoferrin. Although they would have identified the 1 patient with Crohn's disease, this patient would have been identified using traditional testing (i.e. hemoglobin and albumin). In addition, there were many false positive calprotectin results. False positives have the potential to confuse the diagnosis and lead to further, unnecessary testing.

## 1080

### Multi-Specialty Functional Bowel Center Outcomes in Irritable Bowel Syndrome

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**Purpose:** To describe population seen in a multi-disciplinary Functional Bowel Center (FBC) and the impact of the center in the treatment of moderate to severe irritable bowel syndrome (IBS) patients.

**Methods:** Retrospective chart review of 150 patients' charts enrolled (2001 – 2006) at the FBC. The FBC is a multidisciplinary center involving Gastroenterology, Nutrition, Psychiatry, Spirituality and Alternative Medicine specialists. Data extractor was used to collect demographic, medical, surgical and psychiatric histories, and the evaluations and treatments pre and post FBC encounter. Institutional IRB approval was obtained.

**Results:** Population description as follows: 97% Caucasian, 2.6% AA, 123 females (average age 44.1), 27 males (average age 45.5). 73% of men and 43% women had > 5 years of complaints. IBS sub-typing was as follows: Constipation predominant (57.8% of females and 38.4% of males), Diarrhea predominant (29.6% of females and 30.7% of males), Alternating type (6% of females, 3.8% of males), with uncategorized IBS (6% females and 19% males). 7% of patients found alternate diagnosis (IBD, gastric sarcoid, ITP with splenomegaly, severe pan-motility disorders, bacterial over-growth, sprue, and a neurological pain issue).

Psychiatric evaluation found 88% of women (56% pre-enrollment) and 88.4% of men (50% pre-enrollment) had a psychiatric issue (depression/anxiety and adjustment disorders were predominant). 18% of patients were

found to have eating disorders (predominantly binge-eating) and obesity was noted in 34.6% of males and 19% of females. 79% of women and 46% of men had undergone related surgeries in the past. The most common surgery was hysterectomy in females and gall bladder surgery in males.

Most common medication treatment was PPI (95%). The average number of evaluation procedures & imaging was <1/patient after FBC enrollment. Perceived improvement by both physician and patient on FBC follow-up found only 38% felt improved, showing the difficulty in treating this population.

**Conclusion:** This is one of the first descriptive studies of this size, in the setting of a multidisciplinary FBC population. Unique aspects of this population were the predominance of constipation predominant IBS, high psychiatric comorbidities identified and the association of eating disorders and obesity noted. We are currently in the process of collecting prospective data and utilizing the SCL 90 and IBS QOL questionnaires and other indices to determine the impact of the FBC on this population in more detail.

## 1081

### Effectiveness of a Behavioral Medicine Program on Adolescent Irritable Bowel Symptoms and Resource Utilization

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**Purpose:** IBS is a common health syndrome affecting 10 – 15% of patients, who are estimated to use 30% more of the medical budget than any other disease category. No medical therapy is proven efficacious. Parental influence appears key to the development of IBS in childhood. Contributing factors include poor sleep patterns, lack of exercise and stress. Our hypothesis was that a behavioral medicine program for adolescent patients with IBS and their parents in a group setting will result in an improvement in symptoms and reduced health care utilization.

**Methods:** Our intervention was a program for adolescents identified by pediatric gastroenterologists with IBS, and their parents, consisting of 90 minute consecutive sessions over 3 weeks incorporating exercise, relaxation skills (using self guided imagery, yoga and Pilates), patient and parent education, and a motivational movie of the life of a disabled athlete. Endpoints include change in the visual Likert scale of the modified ROME criteria, (considered the gold standard for IBS assessment) and change in medication use. Therapeutic response to the program was assessed at completion of the 3rd session by a change in Likert score from baseline. To minimize placebo effect, scores were also obtained at 3 and 6 months after completion of program.

**Results:** 61 subjects completed the program. At the time of writing the abstract, completed scores were available for 57 subjects pre-intervention, 42 immediately post intervention, 21 at 3 months and 11 subjects at 6 months. A paired t- test was performed on pre and post intervention scores that were available on 40 subjects, and a statistically significant reduction in each ROME Criterion was demonstrated ( $5.7 \pm 1.98$  vs.  $4.0 \pm 2.23$   $P = 0.003$ ,  $3.1 \pm 2.84$  vs  $2.0 \pm 2.24$   $P = 0.000$ ,  $3.6 \pm 2.86$  vs  $2.4 \pm 2.16$   $P = 0.002$ ,  $4.1 \pm 2.68$  vs  $3.15 \pm 2.32$   $P = 0.002$ ). Mean total Likert scores were  $14.6 \pm 8.48$  at baseline,  $11.1 \pm 6.85$  post intervention,  $8.9 \pm 6.65$  at 3 months and  $11.1 \pm 8.72$  at 6 months. Reduction in Likert scores was found to be statistically significant post intervention and at 3 months by repeated measures ANOVA ( $P = 0.006$ ). No significant difference was found between scores at 3 and 6 months.

**Conclusion:** A behavioral intervention program targeting adolescents with IBS and their parents results in symptomatic improvement that is persistent 6 months after completion of the program. Analysis of data regarding utilization is in progress.

## 1082

### Mucosal Cytokine Imbalance in Irritable Bowel Syndrome (IBS)

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**Purpose:** The diagnosis of IBS currently relies solely on patient history and the exclusion of the many disorders which may share its symptomatology; no reliable validated biomarker exists. Recently, however, evidence for immune activation, including alterations in systemic levels of certain cytokines, has been reported in IBS. However, the immune status of the intestinal mucosa, in IBS, remains relatively unexplored. Our aim was to systematically examine mucosal biopsies for changes in cytokine gene expression and protein secretion.

**Methods:** The study population consisted of 59 females with IBS and 39, otherwise healthy, female volunteers attending for colonoscopy. Colonic biopsies from subsets of these were studied by microarray analysis (IBS N = 9; controls N = 8), quantitative RT-PCR (IBS N = 22; controls N = 21), and *ex vivo* biopsy culture (IBS N = 28, controls N = 10). Biopsies from patients with active colitis were used as inflammatory disease controls (IBD; Ulcerative colitis, UC N = 20; Crohn's CD N = 8).

**Results:** While, as expected, gene array analysis revealed extensive overlap between controls and IBS patients, a reduced expression of genes linked to chemokine function was evident among the IBS patients alone. Differential expression was confirmed by quantitative RT-PCR, or *ex vivo* biopsy culture for 5 of 6 selected genes. Reduced secretion of chemokines (IL-8, CXCL-9 and MCP-1) but not pro-inflammatory cytokines (TNF- $\alpha$ , IL-6 and IL-1 $\beta$ ) was established on the basis of results from the *ex vivo* biopsy cultures. These findings, in the IBS patients, were in marked contrast to changes in expression of the same cytokines in the patients with active IBD where there was increased production of both chemokines and proinflammatory cytokines.

**Conclusion:** Despite the expected heterogeneity of the disorder, differences in mucosal chemokine signalling were evident in this cross-sectional study of IBS patients, at the level of both gene expression and protein secretion, with IBS patients demonstrating a consistent deficit in the expression and secretion of chemokines known to play a critical role in mucosal defence.

## 1083

### Test of Brain-Gut Axis in Humans Using Cortical Evoked Potentials and Trans-Cranial, Trans-Lumbar, and Trans-Sacral Magnetic Stimulation and Its Reproducibility

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**Purpose:** Cortical Evoked Potentials (CEP) following anorectal electrical stimulation, and Trans-cranial (TC-MEP), Trans-lumbar (TL-MEP) and Trans-sacral (TS-MEP) motor evoked potentials (MEP) following magnetic stimulation may assess cortical and brain gut interactions, but has not been comprehensively evaluated.

**Aim:** To examine the feasibility and reproducibility of CEP, TC-MEP, TL-MEP and TS-MEP tests.

**Methods:** Five healthy humans (3 females, mean age 38 years) underwent a baseline assessment (Test 1) followed by a repeat assessment (Test 2) after 3 months. Afferent pathway was assessed by CEP following electrical stimulation of the anus and rectum with a probe containing 2 pairs of bipolar ring electrodes. CEPs were recorded (Cz-Fz) at 2000 Hz with an epoch duration of 500 ms. Efferent brain-gut function was assessed by recording rectal and anal MEPs following magnetic stimulations with 70 mm coil (Magstim®) at 80–100% intensity, positioned over each side; 1–3 cm around the vertex of the skull (TC-MEP), 5 cm lateral to the spinal cord at L4-L5 (TL-MEP), and 5 cm lateral to S1-S3 (TS-MEP). CEP responses (P1, N1, P2, N2) were analyzed and the onset of N1 (ms) was used to determine CEP latency. Amplitude was measured as peak-to-peak voltage (mV) of evoked response.

**Results:** Mean data for tests 1 and 2 are shown in Table. Bland-Altman plots showed good agreement between tests for the CEP latencies and for transcranial, translumbar and transsacral MEPs, with a coefficient of variation (CV) of <10% (standard deviation < 10% of mean). The amplitude of CEP and MEP responses showed modest agreement (CV = 15–25%).

**Conclusion:** Combined CEP and MEP studies are feasible and reproducible, both for mapping the entire brain-gut pathway as well as the regional brain-gut segments. This test of brain-gut axis is a simple, inexpensive and valid method of examining anorectal-cortical physiology and may facilitate detection of segmental dysfunction in colorectal disorders.

	Latencies (ms)		Amplitude ( $\mu$ V)	
	Rectum	Anus	Rectum	Anus
	Test 1, Test 2	Test 1, Test 2	Test 1, Test 2	Test 1, Test 2
TC-MEP	21.5, 20.3	21.7, 22.4	16, 34	20, 31
TC-MEP	3, 3.2	3.2, 3.6	15, 24	20, 24
TS-MEP	2.5, 2.6	2.8, 2.9	18, 19	20, 26
CEP	104, 99	106, 101	4.8, 5.5	3.2, 4.0

## 1084

### What Do Internal Medicine Residents Know about Irritable Bowel Syndrome?

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**Purpose:** To assess the ability of internal medicine residents to diagnose and manage irritable bowel syndrome.

**Methods:** Eight multiple-choice question survey of forty three residents. 1. Which of the following clinical criteria is most appropriate for diagnosing irritable bowel syndrome? 2. What is the prevalence of irritable bowel syndrome in the general population? 3. Is irritable bowel syndrome a diagnosis of exclusion? 4. For patients diagnosed with irritable bowel syndrome, which of the following is the best recommended diet modification? 5. Of the patients diagnosed with irritable bowel syndrome, what is the likelihood that these patients have real organic disease? 6. Is a colonoscopy required to make a diagnosis of irritable bowel syndrome? 7. Alosetron, a 5HT-3 antagonist, is used as a treatment for diarrhea predominant irritable bowel syndrome. However, its use is limited because of...? 8. What are the initial laboratory tests recommended by irritable bowel syndrome experts?

**Results:** 13% (6 residents) knew the names of the diagnostic criteria. 46% (20 residents) were aware of the prevalence of irritable bowel syndrome (1). However, only 13% (6 residents) were aware that irritable bowel syndrome is not a diagnosis of exclusion(2). 44% (19 residents) were aware of the recommended dietary modification in irritable bowel syndrome. 20% (10 residents) were aware of the prevalence of organic disease in patients with irritable bowel syndrome and when asked whether a colonoscopy was required to make a diagnosis of irritable bowel syndrome, 16% (7 residents) answered yes; 67% (29 residents) answered no; while the remaining 16% answered variable (1). 11% (5 residents) knew ischemic colitis was an adverse reaction to alosetron. No resident was able to correctly identify the initial laboratory tests recommended by irritable bowel syndrome experts (2).

**Conclusion:** Internal medicine residents are suboptimal in all aspects of irritable bowel syndrome. With the proposed changes in ambulatory medicine and block scheduling (3), we believe gastroenterologists should play a central role in subspecialty ambulatory training. 1. Brandt, L et al, Systematic Review on the Management of Irritable Bowel Syndrome in North America. Am Jour of Gastro Vol. 97, no.11 Sup 2002. 2. Bates, B, IBS Diagnosis Controversial, Despite Guidelines, Internal Medicine News, Jul 15th 06; 58. 3. Fitzgibbons, J et al, Redesigning Residency Education in Internal Medicine: A Position Paper from the APDIM. Ann Intern Med, Jun 06; 144: 920 – 926.

1085

**Prevalence of Irritable Bowel Syndrome in an Older Bi-Racial Population**

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**Purpose:** There is limited data on the prevalence of irritable bowel syndrome in the elderly, particularly among older blacks. In a large community study of elderly, we describe the prevalence of irritable bowel syndrome and its association with age, gender, race and education.

**Methods:** Study subjects are participants in the Chicago Health and Aging Project, a population based study of residents aged 65 years and older of a geographically defined area. In the period 2002–2005, 5273 in-home interviews were administered. The interview included items on gastrointestinal symptoms applying the ROME II criteria.

**Results:** Irritable Bowel syndrome was seen in 225 of 4058 participants yielding an overall prevalence of 4.3%. In a logistic regression model including terms for age, gender, race and education we found the prevalence of irritable bowel syndrome was significantly higher with female gender (OR = 1.4; 95% CI; 1.04,1.9), black race (OR = 2.0; 95% CI 1.4, 2.8), increasing age (OR = 1.02; 95% CI 1.001,1.04) and lower education (OR = 0.78; 95% CI 0.63,0.96).

**Conclusion:** The prevalence of irritable bowel syndrome may be higher in females, blacks, and individuals with lower educational attainment.

Multiple-Adjusted Odds ratios (95% confidence interval)  
for Prevalence of IBS by age, sex, race and education.  
Chicago Health and Aging Project 2002–2005.

	Odds Ratio; (95% CI)	
Age (years)	1.02; (1.001, 1.04)	$P = 0.04$
Female Sex	1.4; (1.04, 1.9)	$P = 0.03$
Black Race	2.0; (1.4, 2.8)	$P < 0.0001$
Education	0.78; (0.63, 0.96)	$P = 0.02$

1086

**Pregabalin Ameliorates Abdominal Pain from Adhesions**

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**Purpose:** Abdominal pain from adhesions is a common post-surgical problem. Re-operation for this condition does not afford long-term pain relief in most patients. Many patients require life-long narcotic therapy that reduces their quality of life. Pregabalin is a drug that is structurally related to gabapentin but has linear pharmacokinetics in the therapeutic range and is FDA approved for the treatment of conditions with neuropathic pain such as postherpetic neuralgia. We have successfully treated patients with abdominal pain from adhesions with gabapentin for many years. The purpose of this study was to determine if pregabalin ameliorates abdominal pain from adhesions.

**Methods:** We designed a double blind placebo controlled 12-week crossover study with pregabalin to treat patients with abdominal pain and documented adhesions and a negative evaluation for chronic abdominal pain. The first 8 weeks is a randomized placebo controlled trial. During the final 4 weeks all patients are offered open label pregabalin. The primary objective of the study is to determine whether pregabalin demonstrates a statistically significant reduction in abdominal pain as recorded on an 11 point Likert scale. The secondary objective is to determine improvement in average daily sleep scores (0–11).

**Results:** 13 patients have enrolled in the study and 8 patients have completed the open label portion. Because we have seen marked improvement in

patients on open label pregabalin, we report the open label findings to date. The pre-treatment mean pain score was 6.09 SD 0.86 and the post-treatment mean was 2.08 SD 1.97 (paired  $t$  test = 0.001). 7/8 patients had a mean drop in daily pain score during the open label treatment by 2 points and 6/8 had a mean drop of at least 3 points. The pre-treatment sleep interference score was 5.08 SD 1.11 and the post-treatment mean was 1.48 SD 1.64 (paired  $t$ -test < 0.001). 7/8 patients had a mean decline in daily sleep score of at least 2 points.

**Conclusion:** The open label portion of the trial suggests that pregabalin may be an effective treatment for abdominal pain from adhesions. Further conclusions await the results of the randomized blinded portion of the study.

1087

**Satisfaction with Laxatives in Chronic Constipation (CC) and Irritable Bowel with Constipation (IBS-C)**

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**Purpose:** Determine frequency of using laxative regimens, perceptions of effectiveness, and satisfaction with laxative treatment in patients with CC and IBS-C.

**Methods:** HMO patients were recruited into 2 groups: those with a clinical diagnosis of constipation (564.0×) in the last year vs. those without a diagnosis of constipation for the previous 5 years. Questionnaires identified subjects in both groups meeting Rome III criteria for CC or IBS-C. Subjects with CC or IBS-C but without a medical diagnosis of constipation were designated non-consulters. This was a postal survey.

**Results:** There were 444 CC subjects and 318 IBS-C (consulters and non-consulters pooled). Groups were similar in race, ethnicity, education, and income. However, CC were older (mean age 70 vs. 61 years,  $P < 0.001$ ) and more likely to be male (34% vs. 21%,  $P < 0.001$ ) and widowed (20% vs. 13%,  $P = 0.01$ ).

CC were more likely than IBS-C to consult physicians (53 vs. 41%,  $P = 0.001$ ) and less likely to use prescription laxatives (14% vs. 20%,  $P = 0.01$ ), over-the-counter laxatives (24% vs. 37%,  $P < 0.001$ ), fiber supplement (28% vs. 44%,  $P < 0.001$ ), herbs (5% vs. 12%,  $P = 0.002$ ), special diets (8% vs. 20%,  $P < 0.001$ ), alternative therapy (0.5% vs. 4%,  $P = 0.001$ ), exercise (17% vs. 29%,  $P < 0.001$ ) or lifestyle changes (3% vs. 6%,  $P = 0.02$ ). When they did use laxatives, CC reported greater satisfaction (55% vs. 36% very or extremely satisfied;  $P = 0.004$ ) and less severe side effects (SEs; 3% vs. 13% very or extremely severe;  $P < 0.01$ ). There were no differences in effectiveness (44% vs. 40% calling laxatives very or extremely effective;  $P = 0.21$ ).

When consulters were compared to non-consulters within the CC and IBS-C groups, there were no differences in effectiveness, SE severity, or satisfaction with laxatives.

Ordinal regression tested the combined effects on satisfaction with laxatives of age, gender, race, consultation, diagnosis (CC vs. IBS-C), severity of SEs, and perceived effectiveness. Significant predictors were perceived effectiveness ( $P = 0.001$ ), SE severity ( $P = 0.001$ ), and diagnosis ( $P = 0.012$ ). Total variance explained was 57.7%.

**Conclusion:** Laxatives are equally effective in CC and IBS-C, but subjects with CC have less severe SEs and are more satisfied with laxative treatment. [Supported by Novartis Pharmaceuticals & R24 DK67674].

1088

**High Dose Dexamethasone for Acute Idiopathic Gastroparesis**

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**Purpose:** The management of acute idiopathic gastroparesis continues to be a challenge for many practicing physicians. Antiemetics and prokinetic agents (dopamine-2 antagonists, 5-HT<sub>4</sub> agonists, macrolides) are commonly considered first line therapy, but may provide only marginal benefit. In addition tolerance and untoward side effects limit their long-term use.

High dose dexamethasone alone or in combination with antiemetics is a mainstay in the treatment of chemotherapy induced nausea and vomiting, but to our knowledge has not been shown to be effective for idiopathic gastroparesis.

We report 3 patients that presented with nausea, vomiting and gastroparesis refractory to antiemetics and prokinetics. The duration of symptoms ranged from 2 weeks to 2 months prior to the initiation of therapy. Patients 1 & 2 received an exhaustive work-up that included Computed Tomography (CT) and Magnetic Resonance Imaging of the brain, as well as CT scans of the abdomen and pelvis. Patient 3 was 18 weeks gestation at the time of evaluation, and declined radiographic imaging. Evaluation of all diagnostic information failed to result in a diagnosis. Gastric emptying scintigraphy with 99mTc colloid-labeled egg sandwich in patients 1 & 2 showed less than 23% and 19% gastric emptying at 2 hours. Both were started on parenteral nutrition after no initial improvement.

Dexamethasone 4 mg intravenously twice daily was eventually started in all three patients and resulted in prompt resolution of symptoms within 72 hours. All patients were eventually converted to the oral dexamethasone and discharged with a tapering dose over several weeks. All three patients remained asymptomatic at 8 week follow up.

We conclude that high dose dexamethasone may be a safe and effective adjunct to standard first-line therapy in the treatment of refractory idiopathic gastroparesis. Further investigation to determine its direct effects on gastric emptying is warranted.

## 1089

### Predictors of Response in Gastroparesis

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**Purpose:** Natural history and outcomes of gastroparesis are not well known and the response to treatment is variable. We aim to determine which clinical features could help identify patients with response to therapy.

**Methods:** 69 patients were included. Symptoms were scored using the Gastroparesis Cardinal Symptom Index, a validated scale of severity that utilizes three clusters (nausea/vomiting, post-prandial fullness/satiety, and bloating). Gastric emptying was measured using a standard 4-hour low fat solid meal. Treatment included conservative measures like antiemetics, prokinetics, antidepressants, analgesics. Interventions included enteral feeding and pacing in selected patients. Response to treatment was defined as overall change in GCSI score of 33% or more as compared with baseline.

**Results:** 29 out of 69 patients had diabetes. 40 had idiopathic gastroparesis. 49 were responders (71%). 20 were non responders (29%). Amongst responders 17 (34.69%) patients required enteral feeding and 10 (20.41%) patients underwent enteral placement as opposed to 8(42.11%) and 4(21.05%) respectively in non responders. 52 patients had delayed gastric emptying (75%). Proportion of responders was not different amongst patients with delayed or normal emptying. Demographic characteristics or subtype of gastroparesis (diabetic/idiopathic) did not significantly differ among responders and non-responders. Baseline scores for nausea, vomiting and retching were similar. However, baseline scores for early satiety ( $P = 0.02$ ), postprandial fullness ( $P = 0.05$ ), stomach distension ( $P = 0.0001$ ) and bloating ( $P = 0.01$ ) were significantly greater in non-responders.

**Conclusion:** Majority of patients with gastroparesis improve with therapy. Specific symptoms seem to be of a predictive value, with severity of early satiety, postprandial fullness, stomach distension and bloating being significantly higher in non responders than responders. On the other hand, neither

the type of gastroparesis nor gastric emptying pattern appeared to predict response. Future studies are needed to investigate whether the clinical phenotype of non-responders is associated with distinctive changes in gastric pathophysiology.

## ENDOSCOPY

### 1090

#### Colonoscopy Outcome Can Be Improved by Using Multiple Assessment Criteria

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**Purpose:** An audit of colonoscopy performance in our unit, using Endosoft® database.

**Methods:** A retrospective audit of colonoscopy practice, Jan- June 2006, for these criteria: 1) Completion rate: Completion of colonoscopy to cecum, terminal ileum or surgical anastomosis, regardless of bowel prep or stenosing lesion. 2) Histology proven lesion rate: Composite standard, incorporating lesion identification, excision or biopsy, retrieval and positive histology for colorectal cancer or adenoma. 3) Use of sedation and analgesia: Mean dose per procedure of midazolam and pethidine, for every endoscopist.

**Results:** 1) The unadjusted completion rate 82.5 percent, (significantly different among 10 endoscopists, range 64.71% to 90.43%), (Pearson Chi Sq 30.08, Degrees of Freedom 9 p0.000). 2) The histology proven lesion rate 10.36, (range 1.96 to 17.95). Difference among endoscopists was not significant, (Pearson Chi Sq 5.41, DF 9  $P = 0.79$ ). total number 181 and it is likely that it lacks power. 3) The mean dose of midazolam for all procedures 3.26 mg, (range of mean 2.31 to 4.36). On analysis of variance:  $F 1.18 P = 0.299$ . The mean dose for pethidine 33.84 mg, (range of mean 25.8 to 43.3) On analysis of variance;  $F 1.67 P = 0.076$ . There was no significant difference for either drug 4) The correlation of midazolam and pethidine doses: Positive, the adjusted R sq 0.18 and Probability of  $F 0.000$ . (Linear Regression). so when a higher dose of one drug associated with higher dose of the second drug was used. 5) The completion rate was not correlated with dose of pethidine and midazolam. (Binary Logistic Regression). The odds ratio with CI: Pethidine 1.00 (0.9933306 to 1.022065), Midazolam 0.9469825, (0.7909089 to 0.133855) 6) The histology proven lesion rate was positively related to completion rate. The weighted measures for total procedures were highly correlated with R square of 0.72 and probability of  $F 0.001$ .

**Conclusion:** There is a significant variation in colonoscopy performance. Smaller doses of sedation and analgesia are used as compared to the past. Use of larger dose of one drug is associated with a larger dose of the other. Better performance in completion is not associated with use of higher dose of medications. Lesion detection and performance in completion are positively correlated. A cumulative rank table in these performance criteria may be used to monitor and improve outcomes.

### 1091

#### Endoscopic Necrosectomy as a Primary Treatment Modality for Pancreatic Abscess

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**Purpose:** Previous case series have reported successful treatment of pancreatic abscess and necrosis with repeated necrosectomy in non-operative candidates. We report our experience with endoscopic necrosectomy in a single session as a primary modality in treating six patients with pancreatic abscess.

Patient Characteristics and Outcomes

Age/Etiology	Abscess Size (cm)	Total LOS	Post Procedure LOS	Complete Resolution/Asymptomatic/Unrestricted Diet (months)
54/biliary	8.5 × 2.7	10	8	TPN; intermittent nausea/abd discomfort; 2.4 × 6.6 cyst (1)
62/biliary	18 × 9	10	8	yes (5)
16/biliary	13.1 × 6.8	15	6	yes (3)
36/biliary	17 × 8 with extension into psoas	24	24	IDDM, pancreatic enzymes (3)
77/biliary	10 × 1.3	27	24	yes; 2.3 cm cyst (4)
43/idiopathic	13.5 × 6.9	18	4	yes; small ill-defined area (9)

LOS: length of stay

**Methods:** Six patients with pancreatic abscesses between April 2006 and February 2007 were offered endoscopic necrosectomy as primary treatment. All patients were informed of the limited experience with this approach and informed that surgical intervention is considered standard of care. Utilizing a linear array echoendoscope, a site was selected free of intervening vessels. Transmural puncture was performed with a 19 gauge needle followed by insertion of a 0.035 inch guidewire into the abscess. After sequential dilation over the wire the echoendoscope was exchanged for a standard gastroscope, which was used to enter the abscess. A single session necrosectomy was performed with a standard snare, retrieval net and/or biopsy forceps. Upon completion of the necrosectomy, two double-pigtailed stents were placed.

**Results:** See table 1. Surgery was avoided in all patients. The median size of abscess was 13.3 cm. Three of the patients had undergone cystgastrostomy stent placement prior to the necrosectomy. Nasocystic lavage was performed in 4 of the 6 patients. There were no peri-procedural complications. Mean follow-up was 3.5 months. Four of the 6 are tolerating an unrestricted diet and all have noted an increase in weight. Three of the 6 have completely resolved fluid collections on repeat CT scan. One patient developed insulin dependent diabetes and requires pancreatic enzymes for steatorrhea. One patient developed an ulcer at the cystgastrostomy site, resulting in a minor gastrointestinal bleed that was treated without complication.

**Conclusion:** Endoscopic necrosectomy appears safe and effective as a primary treatment in patients with pancreatic abscesses. Randomized studies are warranted.

group than antibiotic group. RR for any of the above mentioned complication was 2.02 times higher in placebo group than antibiotic group.

**Conclusion:** Antibiotic prophylaxis prior to ERCP reduces the incidence of bacteremia, cholangitis and sepsis substantially. Our analysis concludes that the routine use of antibiotic prophylaxis should be recommended for all patients undergoing this procedure with a therapeutic intension, as no one does diagnostic ERCPs any more. The Choice of antibiotics used is based on published national guidelines, as well in keeping up with the local microbiology results and trends in the specific medical institution, which is revised on annual basis. In our own institution, we give one dose of IV unasin 3 grams IV prior to the procedure; alternatively IV gentamycin (5 mg/Kg) and vancomycin (15 mg/Kg) are used if patient is allergic to penicillins.

Key word: [Antibiotic prophylaxis, ERCP, cholangitis, sepsis, relative9 risk]

## 1092

### Prophylactic Antibiotic Usage in Endoscopic Retrograde Cholangiopancreatography (ERCP): A Meta-Analysis and Systematic Overview

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**Purpose:** Considerable controversy exists regarding the role of prophylactic antibiotic administration prior to endoscopic retrograde cholangiopancreatography (ERCP). The aim of this meta-analysis is to analyze the data in order to determine whether antibiotic prophylaxis reduces the rate of occurrence of bacteremia and/or the rate of sepsis/cholangitis among patients undergoing ERCP.

**Methods:** Using PubMed, Medline, Embase, Current Contents, and the Cochrane Database of Systematic Reviews databases (OVID), a literature search was performed for papers published from January 1980 to December 2006. All retrieved papers comparing aforementioned outcomes with and without prophylactic antibiotic before ERCP were rated according to the strength of evidence and carefully analyzed.

**Results:** A total of 9 studies met the inclusion criteria for the meta-analysis. All the studies were randomized and prospective. Total of 1547 subjects were included in the analysis. 764 (49%) received prophylactic antibiotics and 783 (51%) received placebo. There was no statistical significant difference between the two groups at base line. Relative risk (RR) for bacteremia was 2.65 times higher and for cholangitis/sepsis was 1.76 times higher in placebo

## 1093

### A Simple Method for "Spontaneous" Colon Decompression during Colonoscopy

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**Purpose:** To describe a simple method for colon decompression during colonoscopy. The anecdotal benefits of this maneuver are described.

**Methods:** During colonoscopy, if ambient air is utilized as the insufflating agent, this may be associated with more prolonged post-procedure cramping and belly distention. I have devised a method for simple, "spontaneous" colon decompression, which I employ routinely as the colonoscopic procedure is nearing completion (and at times, earlier during the procedure). I term this "spontaneous," as it does not involve use of endoscopic suction.

During colonoscope withdrawal, the rubber biopsy valve is removed from the instrument channel port, which is located on the end of the endoscope grip section (and a gauze pad is placed over the area), to allow spontaneous passage of colon gas to the atmosphere. I sometimes place my right hand over the abdomen (while the colonoscope is being held with the left hand), and gentle transabdominal pressure usually facilitates more voluminous "spontaneous" transendoscopic gas egress. Sometimes, a couple of "taps" on the suction valve are used to initiate gas egress (the suction channel sometimes needs to be cleared of debris).

**Results:** By repeating this maneuver a few times during the withdrawal phase of colonoscopy, the patient usually reaches the recovery area more comfortably, and with minimal if any belly distention. The maneuver is also employed after traversing a "difficult sigmoid"-when rapid proximal colon decompression is desired to avoid the potential effects of barotrauma. I also find the maneuver particularly helpful after a prolonged procedure, or one in which a large polyp was removed in piecemeal fashion. Hearing the prominent "spontaneous" passage of colon air through the instrument channel port gives me certitude that perforation is very unlikely to have occurred. Under the circumstances outlined, the colonoscope is simply acting as a "pressure bridge" between the colon and the atmosphere (the anal sphincteric mechanism is now not acting as a resistive factor to colon decompression). In this situation, free egress of air through the colonoscope, in association with the

patient having a soft belly at the conclusion of colonoscopy, gives me- satisfaction and certitude, my patient-more comfort, and the nurse overseeing recovery-a less painstaking task.

**Conclusion:** The "spontaneous" colon decompression method described above is a useful adjunct to the standard colonoscopic procedure. It is easy to perform, safe to employ and provides the multiple potential advantages noted.

## 1094

### Prospective Colonoscopy Major Complication and Completion Rates by a Community Practitioner

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**Purpose:** To report prospective data relating to colonoscopy major complication and completion rates by a single community practitioner.

**Methods:** Study includes results relating to all colonoscopic procedures performed by a board-certified community gastroenterologist (in practice 16 years). Exams were performed between 2/1/06 and 3/15/07. Informed consent was obtained prior to each procedure. Olympus instruments used included CFQ160L, CFQ180AL, PCF140L and on 4 occasions, GIFQ160L. Instrument was chosen at the discretion of the endoscopist, who was able to change endoscopes. Patients avoided ASA/NSAID's for 7 days prior to elective examinations. Warfarin anticoagulation was managed according to guidelines. Polyps <1 cm were most often removed with cold-snare. Major complications were prospectively captured utilizing mechanisms in place at the community hospital and outpatient office endoscopy unit (OEU), where > 99% of colonoscopic procedures were performed. At the hospital, the QI department routinely screens all hospital admissions, as well as charts of patients continuously hospitalized for major complications (including post-procedure hemorrhage, perforation, cardiorespiratory events, events requiring surgical management and post-polypectomy syndrome). Prospective monitoring is also in place in the OEU [3-day post-procedure phone interview and 30-day patient satisfaction mailing (includes questions which would trigger further investigation if a complication was suspected)] to capture major procedure-related complications. Patients were provided with phone contact information and written instructions relating to signs and symptoms, which would suggest a possible complication. Colonoscopy completion was documented by the gastroenterologist performing the procedure. "Completion" required intubation of the cecum or passage of the colonoscope to the ileocolonic anastomosis, and was documented by photographs (appendiceal orifice, ileum, ileocecal valve, ileocolonic anastomosis or any combination). **Results:** From 2/1/06 to 3/15/07, 1403 colonoscopic procedures were performed. Colonoscopy was complete in 1391/1403 = 99.1%. Reasons for an incomplete exam included: diverticular disease (4), poor preparation (3), severe ischemic colitis (2), malignant obstruction (1), abdominal wall hernia (1), obesity/colon redundancy (1). (1) major complication (post-polypectomy hemorrhage) occurred.

**Conclusion:** Colonoscopy can be performed safely in the community setting and with results comparable to those published by experts in academic settings.

## 1095

### ERCP-Associated Pancreatitis: Systematic Evaluation of 99,483 ERCP Procedures with Qualitative Meta-Analysis

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**Purpose:** ERCP-associated pancreatitis (EAP) is a serious complication of ERCP. Contradictory data exist regarding prevention of ERCP. We did a systematic eval of 99,483 ERCP procedures with qualitative meta-analysis (Meta-ethnography).

**Methods:** PubMed Search for ERCP with no language barrier (1995–2006) was done. Also PubMed Search for "PostERCPpancreatitis" was done. More

papers on EAP were added manually. Depending on the quality, trials were classified Level 1–4. Meta-ethnography by Qualitative research methods was performed (Eval Rev 9:627–643, 1985; The Lancet 358:483–488, 2001)

**Results:** From 1995 to 2006, there were 6140 citations for ERCP; 5193 (85%) were in English. There were 203 citations for EAP; 29 more papers on EAP were added manually. Detailed eval of 232 papers was done: Summary sheets were created. The total no. of ERCP procedures was 99,483; EAP occurred in 4535 (4.5%, range 0.2–33%; Median 6.2%) cases. Gender info was available in 34,951; 20,062 (57%) were women. Mean age was 55.6 yrs. Pharmacologic interventions to prevent EAP included somatostatin, Octreotide, gabexate, ionic vs non-ionic contrast media, prednisone, allopurinol, hydrocortisone, glucagon, calcitonin, atropine, n-acetylcysteine, nifedipine, glyceryl trinitrate, 5FU, Lidocaine or epinephrine spray, botulinum toxin, ulinastatin, aprotinin, beta-carotene, S.Q. heparin, diclofenac, indocin (Rect Supp), secretin, prophylactic antibiotics, interleukin-10 antag, monoleukast Na, H-2 receptor antag, CCK antag, lexipanthate (PAF inhibitor) & oral tetracycline. In general pharmacologic methods were ineffective: somatostatin, gabexate, Ulinastatin showed promise. Osmolality of Contrast media had no effect on EAP. Endoscopic methods included suprapapillary needle puncture, transpapillary septotomy, biliary sphincterotomy, prophylactic pancreatic stent (PPS). The PPS seems effective in preventing EAP: however a failure to put an attempted SSP more likely will result in SEVERE EAP. The risk factors for EAP are: female gender, young age, precut sphincter, balloon dilation of papilla, SOD, difficult cannulation, pancreatic injection, normal bilirubin, previous h/o EAP.

**Conclusion:** The frequency of EAP is 4.5%; range 0.25 to 33%; median 6.5% Pharmacologic methods to prevent EAP unsatisfactory. PPS is effective but has important caveat. Risk factors for EAP should be recognized.

## 1096

### Endoscopic Ultrasonographic Evaluation of Hemodynamics in Esophageal Variceal Patients Related to Early Variceal Relapse

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**Purpose:** We evaluated retrospectively the hemodynamics of esophageal varices before and after endoscopic injection sclerotherapy (EIS) and investigated the influence of hemodynamics on variceal recurrence as revealed by endoscopic color Doppler ultrasonography (ECDUS).

**Methods:** Patients were divided according to those with early recurrence (Group A, N = 16) and those without recurrence over the long-term (Group B, N = 12), and those without recurrence between 1 and 3 years (Group C, N = 281). All 309 cases were examined by ECDUS before EIS and 3–5 months after EIS. We monitored the color flow images of blood vessels of paraesophageal veins (PEV), perforating veins (PFV), and cardiac intramural veins (CV) with ECDUS. PEV were classified as either shallow PEV or deep PEV, and PFV were classified as either the inflowing or the outflowing type or mixed type.

**Results:** Before EIS, the detection rates of blood flow in Group A were 16/16 (100%) for PEV, 12/16 (75.0%) for CV, and 13/16 (81.3%) for PFV. PFV were inflowing type in 10 of 13 cases. The detection rates of blood flow in Group B were 12/12 (100%) for PEV, 9/12 (75.0%) for CV, and 6/12 (50.0%) for PFV. PFV were inflowing type in 3 cases and outflowing type in one case, and mixed type in 2 cases. The detection rates of blood flow in Group C were 281/281 (100%) for PEV, 219/281 (77.9%) for CV, and 131/281 (46.7%) for PFV. PFV were inflowing type in 69 cases and outflowing type in 31 cases, and mixed type in 31 cases. The detection rates by ECDUS of PFV and inflowing PFV in Group A were significantly higher than those in Group B and C before EIS.

After EIS, the detection rates of blood flow in Group A were 16/16 (100%) for PEV, 9/16 (56.3%) for CV, and 5/16 (31.3%) for PFV. PFV were the inflowing type in all 5 cases. The detection rates of blood flow in Group B were 11/12 (91.7%) for PEV, zero/12 (0%) for CV, and 2/12 (16.7%) for PFV. PFV were of the outflowing type in all 2 cases. The detection rates of blood

flow in Group C were 251/281 (89.3%) for PEV, 33/281 (11.7%) for CV, and 6/281 (2.1%) for PFV. PFV were of the outflowing type in all 6 cases. The detection rates by ECDUS of CV, PFV, and inflowing PFV in Group A were significantly higher than those in Group B and C after EIS.

**Conclusion:** ECDUS enables prediction of early recurrence of esophageal varices based on hemodynamic findings before and after EIS.

## 1097

### Natural History of the Mallory Weiss Tear in African-American and Hispanic Patients

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**Purpose:** The Mallory Weiss Tear (MWT) is an important cause of acute upper gastrointestinal bleeding (AUGIB). However it is usually perceived to be a trivial, uncommon and rather benign lesion and often does not claim urgent attention like other lesions such as peptic ulcers and esophageal varices. The literature is scant about the natural history of MWT in African-American and Hispanic patients, which are our predominant clients. Aim of our study was to determine the natural history of MWT in these two ethnic groups.

**Methods:** Medical records of all patients with AUGIB were reviewed retrospectively over a 10-year period (January 1996- December 2005). Patients were excluded if endoscopy was not done. Endoscopic diagnosis of MWT was made in 12% (N = 698) of all patients with AUGIB. The information abstracted included, primary diagnosis, endoscopic findings, clinical and laboratory parameters, associated comorbidity, therapeutic interventions, and outcome over 30 days.

**Results:** Of 698 patients with MWT who presented with AUGIB, 398 (57%) did not have a preceding history of retching or vomiting. Bleeding episode was hemodynamically significant (orthostasis, a drop of hemoglobin < 10 g/dl, and/or >6 U of blood transfused) in 216 (31%) patients. Alcohol, male gender, smoking, substance abuse, chronic kidney disease, coagulopathy, and chronic lung disease were positively correlated with MWT ( $P < 0.0001$ ). Most of the patients with MWT (80%) had an unremarkable and short hospital stay (1-4 days). Recurrent bleeding occurred in 84 (12%) patients, within 30 days. Endoscopic hemostasis was unsuccessful in 77 (11%) patients, 38 (50%) of these patients, required surgical intervention. Overall mortality was 10% (70 patients), 7% (49 deceased patients) being in endoscopic hemostasis failure group. Most of the deaths (85%) occurred in patients with associated comorbidities. There was no significant difference in natural history or outcome of MWT amongst African- American and Hispanic patients.

**Conclusion:** MWT is a significant cause of AUGIB in African-American and Hispanic patients. More than half of our patients with MWT did not have preceding history of retching or vomiting. It can may be associated with rebleeding, significant morbidity and notable mortality.

## 1098

### Predictors of Rebleed in Actively Bleeding Duodenal Ulcer after Endoscopic Intervention in a Developing Asian Country

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**Purpose:** To determine the predictors of rebleeding in patients with actively bleeding duodenal ulcers after combined adrenaline injection and argon plasma coagulation (APC).

**Methods:** Consecutive patients who were admitted from December 2003 to March 2007 with actively bleeding duodenal ulcers were included. Endoscopic intervention with injection adrenaline and APC was done to achieve complete hemostasis. Actively bleeding duodenal ulcers were classified on the basis of Forrest criteria. Primary outcome measure was post intervention rebleed and secondary outcome measure was 30 days mortality.

**Results:** Total of 74 patients were analyzed, who required the endoscopic intervention with injection adrenaline and APC, all achieved initial hemostasis. Mean age was  $53 \pm 16$  years with 79.7% were male. Mean Rockall score before endoscopy was  $2.0 \pm 1.3$  and post endoscopy was  $5.08 \pm 1.3$ . Mean packed cell transfusion was  $2.2 \pm 1.83$ . Out of 74 patients 16(21.6%) rebled. History of NSAID use was in 11 (68.8%). Out of 16 in 8 (50%) hemostasis was achieved endoscopically, while 6 underwent surgery and two needed angio-embolization. Predictors of rebleed on multiple logistic regression analysis are shown in table 1. Overall 30- day mortality occurred in 2 (2.7%) patients, one died of sepsis while other due to posts surgery myocardial infarction.

**Conclusion:** Forrest score 1, large ulcers, high rockall score and ulcers at D1 and D2 junction were independent predictors of rebleed in duodenal ulcers after successful endoscopic intervention.

Independent Predictors of Rebleed in bleeding duodenal ulcers after intervention			
	Adjusted Odd Ratio	95% CI for Adjusted Odd ratio	P-value
Rockall score			
<5	† 1		
≥5	6.5	1.00-43.09	0.04
Site of Duodenal Ulcer			
D1	† 1		
Junction of D1 and D2	8.5	1.23-59.17	0.03
Size of Duodenal Ulcer			
<1.5	† 1		
≥1.5	15.9	3.22-79.15	0.001
Forrest Criteria			
Forrest II	† 1		
Forrest I	7.1	1.32-38.05	0.02

## 1099

### Incidental Findings on Peg Placement May Indicate Procedure Deferment

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**Purpose:** Percutaneous endoscopic gastrostomy (Peg) placement is often performed in cases of persistent refusal to take in adequate intake or with patients with difficulty in swallowing. These patients often suffer from dementia and may be nonverbal. They are unable to communicate pain or discomfort. Swallow studies are performed in part to document the degree of dysphagia and to recommend PEG placement when indicated. Calorie counts are also performed to document poor intake. These studies do not address the underlying etiology for the patients change in appetite. A patients refusal to take in nutrition may be multifactorial. A possible treatable gastrointestinal source may be the cause for the decreased oral intake.

**Methods:** We conducted a retrospective analysis of a 135 consecutive patients. These patients were admitted between 8/03 and 3/05. All patients who underwent endoscopy for the purpose of PEG placement were included regardless if placement was successful. None of the patients had previous peg placement. The study was performed at a university teaching hospital. **Results:** A total of 131 out of 135 procedures were completed with successful PEG placement. Two of the four patients who had placement deferred had endoscopies where adequate landmarks for placement could not be identified. Two previously unknown gastric cancers were discovered at the time of endoscopy in the remaining two patients who had unsuccessful placement. A total of 7 duodenal ulcers, 6 gastric ulcers were noted. Other findings included esophagitis (14), gastritis (28) and duodenitis (13).

**Conclusion:** Serious endoscopic findings are often found while PEG placement is being performed. These findings may often explain why a patient who suffers from dementia may refuse oral intake. Therapy such as proton pump inhibitors may be effective in treating acute gastrointestinal problems



allowing the resumption of adequate oral nutrition. Further prospective studies may be necessary to assess if treating such findings may obviate the need for peg placement.

## 1100

### The Frequency of Intraabdominal Metastasis Identified during EUS Staging for Lung Cancer in a Community Setting

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**Purpose:** Lung cancer staging is performed to determine whether aggressive local therapy (surgery, curative-intent radiotherapy) should be undertaken or if metastasis precludes this approach. Endoscopic ultrasonography with fine needle aspiration (EUS-FNA) of the mediastinum is frequently performed as part of this staging, both to obtain cell type and to identify extent of nodal involvement. The aim of this study was to determine the frequency of pathologically identified intraabdominal metastasis found during EUS-FNA staging of lung cancer in a community setting.

**Methods:** A retrospective review was undertaken of all patients referred to gastroenterology at St. Mary's/ Duluth Clinic, Duluth, MN for EUS lung cancer evaluation/staging from 2003 to 2006. Categorical data were recorded including age, sex, cell type, sites of FNA, and whether pre-EUS imaging (CT/PET) suggested intraabdominal metastasis.

**Results:** 101 individual subjects (70 with non-small cell, 30 with small cell and 1 with mixed non-small cell/small cell cancer) were identified for inclusion. Intraabdominal metastases were confirmed by FNA in 22 subjects, most commonly the left adrenal (10/22, 45%) and the liver (9/22, 41%). Other sites included pancreas, spleen, and abdominal lymph nodes. More than one abdominal site was confirmed in 3 subjects (liver/adrenal, pancreas/adrenal, periduodenal nodes/adrenal). In 7/22 (32%), the intraabdominal disease was not suggested by pre-EUS imaging. Small cell cancer tended to be found in the abdomen more commonly (11/30, 37%) than non-small cell cancer (11/70, 17%), ( $P = 0.08$ ). In 2 cases, CT suggested an abnormal adrenal that was found to be benign by FNA, and these subjects underwent thoracotomy with curative intent resection.

**Conclusion:** Intraabdominal metastases of lung cancer are not infrequent, occurring in 22% of our referral cohort. EUS-FNA identifies and cytologically confirms intraabdominal metastases suggested or missed by CT and thus can dramatically alter patient management. EUS staging of lung cancer should not be limited to the mediastinum and must include a careful examination of intraabdominal structures, with tissue confirmation of suspected metastasis.

## 1101

### Trimming of Migrated Metal Stent for Malignant Colonic Stricture Using Argon Plasma Coagulation (APC)

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**Purpose:** Over the last decade colorectal stenting has been reported as an alternative to emergency laparotomy to relieve malignant colonic obstruction. Complications of colorectal stenting include tenesmus, transient anorectal pain, rectal bleeding, colonic ulceration and perforation and even stent migration. APC has been used to trim metal biliary stents as well as metal colonic stents. Trimming of metal colonic stents has been reported for the indication of tenesmus. We report the first case of trimming of a migrated metal colonic stent for stent induced severe anorectal pain.

**Methods:** We present a case of a 54-year-old female with history of metastatic colorectal carcinoma who had stent placement secondary to obstruction. Subsequent distal migration of the stent caused ulcerations into the rectal mucosa and excruciating anorectal pain. We used APC to successfully trim the exposed distal portion of the metal stent and a rat tooth forceps to retrieve the stent fragments.

**Results:** Upon follow up in one week, the patient reported complete relief of stent induced anorectal pain.

**Conclusion:** The use of APC for trimming metallic stents is an effective procedure that can be used to trim migrated rectal stents that result in significant rectal pain. To date, a few studies have been published that use APC to trim metallic stents placed in the gastrointestinal tract. Most cases of stent trimming with APC have been reported in metallic biliary stents that have migrated distally. Two cases have been reported where a colonic stent was trimmed using APC for the treatment of tenesmus. To the best of our knowledge, ours is the only known case in which the indication for stent trimming was severe stent induced rectal pain. The procedure resulted in complete relief of the patient's symptom. Therefore, APC is a safe and effective way to trim colo-rectal stents to definitively relieve the symptom of stent induced rectal pain in patients who have experienced distal stent migration and mucosal ulceration.

## 1102

### Endoscopic Management of Postcholecystectomy Biliary Leaks

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**Purpose:** Biliary leak is a common complication following cholecystectomy. Endotherapy is an established method of treatment. However, the optimal intervention is not known.

**Methods:** Seventy three patients with postcholecystectomy biliary leaks from July 2000 to April 2007 were retrospectively evaluated.

**Results:** There were 19 males and 54 females with a mean age of 43.06 years. Patients presented 17.95  $\pm$  17.09 days (range 1–90 days) following cholecystectomy (46 open and 27 laparoscopic) with pain abdomen (42), jaundice (21), fever (21), and abdominal distension (37). Bilious abdominal drain was present in 55 patients. Endoscopic retrograde cholangiopancreatography detected leak at cystic duct stump in 35, stricture with mid common bile duct (CBD) leak in 4, leak from right hepatic duct in 2 and ligated CBD in 32 patients. Nine patients also had bile duct stones. One patient had broken "T" tube with stone. Endotherapy was possible in 41 patients and 32 patients with ligated CBD underwent surgery. Two patients with stones, one patient with broken "T" tube with stone and 4 patients with stricture common bile duct with leak were managed with sphincterotomy and stent. Seven patients with cystic duct stump leak with stone were managed with sphincterotomy and stone extraction. Three outdoor patients with cystic duct stump leak were managed with sphincterotomy and stent. Eleven patients with cystic duct stump leak admitted in hospital were managed with sphincterotomy and nasobiliary drain. Thirteen patients had coagulopathy hence sphincterotomy could not be done and were managed with only nasobiliary drain (7) and stent (6). Leak closure could be achieved in 100% patients. Mild pancreatitis occurred in 4 patients who were managed conservatively.

**Conclusion:** Endoscopic intervention is a safe and effective method of treatment of postcholecystectomy biliary leaks. However, management of postcholecystectomy biliary leaks should be individualized based on type of leak and should include stent in outdoor patients and nasobiliary drain in indoor patients with simple leak, sphincterotomy and stone extraction in patients with stone, sphincterotomy and stent in patients with stricture with or without leak and those with ligated duct should undergo surgery.

## 1103

### Laparoscopic-Assisted Double Balloon Enteroscopy in Persistent Obscure GI Bleeding

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**Purpose:** Persistent obscure GI bleeding (OGIB) is a challenging clinical problem. Open intraoperative enteroscopy (IOE), the gold standard in management, has been associated with variable rates of morbidity (0–52%) and mortality (0–11%)<sup>1</sup>. Double balloon enteroscopy (DBE) allows deep intubation and therapeutics in the small bowel, but its success can be limited by bowel fixation from previous surgery. We evaluated the diagnostic yield, complications, and outcome of laparoscopic-assisted double balloon enteroscopy (LAP-DBE) for persistent OGIB when DBE fails to reach a bleeding lesion.

**Methods:** Thirteen patients with planned LAP-DBE for persistent OGIB were identified retrospectively from a prospective database from 8/04 to 3/07. Patient demographics, laboratory studies, DBE and operative reports, and length of stay were reviewed. LAP-DBE was performed under general anesthesia. DBE was performed using standard methods<sup>2</sup>. Laparoscopic instrumentation facilitated lysis of adhesions and advancement of the endoscope around angulations in the small bowel. Lesions were treated with thermal therapy (argon plasma coagulation or bipolar electrocautery), epinephrine injection, endoscopic clips, or surgical resection.

**Results:** Of 13 patients with planned LAP-DBE, 9 patients underwent complete LAP-DBE, 3 underwent laparoscopy only, and 1 underwent DBE only. Bleeding lesions were identified in 11 (85%) of 13 patients, most commonly Dieulafoy's lesions, AVMs, and ulcers. Nine (82%) of 11 patients with identified lesions had partial small bowel resections; 2 (18%) were treated with endoscopic therapy alone. Of two patients with negative LAP-DBE, one rebleed. Four cases were converted from laparoscopic to open laparotomy for further management of the bleeding site. One complication of devascularized small bowel occurred (8%). Mortality rate was 0%. Average length of stay following LAP-DBE was  $5.2 \pm 4.2$  days. Over an average follow-up period of >7 months (range 2–16 mo), 9 (69%) of 13 patients had no further bleeding.

**Conclusion:** 1) LAP-DBE is effective in managing persistent OGIB when standard endoscopy and unassisted DBE have failed to find a bleeding source. 2) Diagnostic and therapeutic yields in this series are comparable to those previously reported for IOE<sup>1</sup>. 3) Average LOS after LAP-DBE was short.

1. Hartmann D et al. *Gastrointest Endoscopy* 2005;61: 826–832.
2. Yamamoto H et al. *Gastrointest Endoscopy* 2001;53: 216–220.

## 1104

### Botulinum Injection for Satiety and Weight Loss

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**Purpose:** To show the efficacy of botulinum toxin injections for satiety and weight loss.

**Methods:** Twelve patients were asked to take pre- and post-procedure gastric emptying studies and to record satiety scores.

We injected 100 units of botulinum toxin into the pylorus.

Patients were followed for four months.

**Results:** Pre-procedure weights were 192.5–506 pounds. At 8 weeks all lost weight. The two with the highest weights, 333.5 and 506, lost the most, 25.5 and 41 pounds.

With these outliers removed, the group's mean weight loss of 1.1 pounds/week was significantly greater than zero ( $P < .001$ , 95% confidence interval [0.6 1.6]). Individual weight loss averaged 0.13 to 2.31/week. Of the eight patients with recorded weights at weeks 14–16, seven lost weight. Mean weight loss for the group of 1.0 pounds/week was significantly different from zero ( $P < .01$ , 95% confidence interval [0.4 1.7]).

Ten patients had pre-procedure emptying studies. Four had T 1/2 times less than 20 minutes ( $N = 78$  minutes  $\pm 11$ ). Four ranged from 26 to 54 minutes. The last was 198 minutes.

With the outlier removed, at 8 weeks these times were weakly associated with weight loss ( $P = .053$ , R-squared .36). With the outlier also removed at 14–

16 weeks, the remaining seven patients' weight loss linearly associated with their emptying times ( $P < .02$ , R-squared .65). Specifically, each increase of 10 minutes of pre-procedure gastric emptying times was associated with a .35 pound per week loss. No significant association was found between post-procedure emptying times and weight loss, nor between pre- and post-procedure difference in emptying times.

All patients reported increased satiety. Nine reported gastroesophageal reflux pre-procedure; all reported improvement after.

One patient had significant abdominal pain and a mildly elevated amylase and lipase which resolved spontaneously in 3 days. Minor side effects varied from belching, dry mouth, food intolerance to fat or fried foods, a variable change in bowel habits, and mild nausea. All patients' symptoms resolved by week 5.

**Conclusion:** Studies have shown faster than normal gastric emptying in the obese as did ours. We also showed that the closer to normal pre-procedure emptying times, the greater the weight loss response to botulinum injections. Our study and 3 others prove that botulinum toxin is safe when injected in the stomach for weight loss. Further research is needed to confirm the correlation between gastric emptying and response to and location of botulinum toxin injection.

## 1105

### Community-Based Helicobacter pylori Screening in Patients with Endoscopic Evidence of Peptic Ulcer Disease

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**Purpose:** Identification of *H. pylori* (Hp) is important in the management of peptic ulcer disease (PUD) as treatment greatly reduces the risk of ulcer recurrence. Our study aimed to identify Hp screening rates in patients with PUD as well as differences in screening and treatment rates between three specialties performing endoscopies: Gastroenterology (GI), Surgery, and Family Practice (FP).

**Methods:** Charts of 715 consecutive inpatients diagnosed with PUD on upper endoscopy in Wichita, KS were reviewed for Hp screening with biopsy or rapid urease testing, biopsy histology, culture, or PCR, fecal antigen, serology, salivary assay, or urea breath testing. Charts of Hp positive patients were reviewed for treatment with an approved regimen while hospitalized or documented plans for outpatient therapy. Comparisons between endoscopist specialties were made using chi-square analysis.

**Results:** 76.9% (550/715) of patients with PUD diagnosed on upper endoscopy were screened for Hp. Of those patients screened, 16.4% (90/550) were Hp positive. While 63.3% (57/90) of Hp positive patients were treated during hospitalization, only 9.1% (3/33) of the remaining untreated patients had documented plans for outpatient treatment. Three endoscopies were performed by Internal Medicine physicians and were excluded from specialty analysis. GI performed 321 endoscopies and screened significantly more frequently [83.5% (268/321)] than surgery [72.1% (261/362)] who screened more frequently than FP [65.5% (19/29)] for Hp ( $\chi^2 = 14.685$ ;  $P = 0.001$ ). No significant differences by age group or gender and type of specialty were identified. Comparison of treatment rates showed that GI treated Hp positive patients significantly more frequently [80.4% (37/46)] than surgery [50% (20/40)] with no FP patients (0/3) receiving treatment ( $\chi^2 = 14.136$ ;  $P = 0.001$ ).

**Conclusion:** While GI screened and treated Hp positive patients more frequently than other specialties, improvement is needed in both areas for all endoscopists. Patients not receiving inpatient treatment need well documented plans for outpatient therapy to ensure adequate follow-up of pending results. Rates of Hp were lower than expected indicating possible false negative test results. As identification and eradication of Hp are important in the prevention of recurrent PUD, potential sources for false negatives on initial Hp testing should be identified so that repeat testing may be performed as indicated.

1106

### Lack of Education and Training in Video Capsule Endoscopy among Pediatric Gastroenterology Fellows

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**Purpose:** Since its approval in August 2001, Video Capsule Endoscopy (VCE) has been performed in over 400,000 patients. The majority of these examinations have been conducted in the adult population, however, this technology has been approved in children greater than 10 years of age since 2003. The primary method of teaching pediatric gastroenterologists-in-training to use this revolutionary technology has been through gastrointestinal society sponsored courses. Presently, however, there are no guidelines or strategies for instructing pediatric gastroenterology fellows how to utilize and interpret VCE studies. This has left individual training programs to develop their own institution-specific ways of incorporating VCE into the existing curriculum. We therefore conducted a survey of pediatric gastroenterology fellows to investigate the prevailing practices of video capsule endoscopy education.

**Methods:** A 10 item questionnaire was both sent via email to pediatric gastroenterology fellows at 35 training programs as well as posted on the electronic pediatric gastroenterology fellows' bulletin board about their use of and instruction in video capsule endoscopy. All responses were kept anonymous and confidential in accordance with the practices of the hospital's Institutional Review Board.

**Results:** As of 2005, there were 175 pediatric gastroenterology fellows nationwide, we received 51 responses (response rate of 29%). VCE is performed in pediatric patients at 82.4% of training programs. Fellows, however, did not routinely participate in performing or interpreting VCE. Fellows ordered a mean of 1.7 VCEs (range 0 to 10), and they reviewed a similar number with an attending physician (mean 1.7, range 0 to 35). Only 17.6% fellows reported receiving formal instruction in VCE, with 76.5% of fellows stating that they would benefit from more teaching. Only 4 out of 51 (8%) of respondents had attended a VCE seminar.

**Conclusion:** As video capsule endoscopy becomes a more widely utilized modality of luminal evaluation in the pediatric population, it is critical that pediatric gastroenterology fellows be trained in this skill. The current system of haphazard education is ineffective and in need of formal guidelines.

1107

### Application of Cyanoacrylate for Hemostasis in a Patient with Refractory Post-Sphincterotomy Hemorrhage

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**Purpose:** To present cyanoacrylate as an alternative means of achieving hemostasis in post-sphincterotomy bleeding.

**Methods:** Case Report

**Results:** A 58 year old male presented to our emergency department with melena 72 hours post-ERCP with sphincterotomy and common bile duct stone removal. In addition, he also had placement of a coronary artery bare metal stent a month prior to the development of choledocholithiasis. Because of the coronary stent, he required aspirin and clopidogrel therapy which was not held for his sphincterotomy.

Upon admission an urgent EGD was performed revealing an actively bleeding sphincterotomy site with adherent clot. Hemostasis was initially achieved with epinephrine, placement of 6 hemoclips, and application of electrocautery. The patient's cardiologist felt the risk of thrombosis of the coronary stent was too high to discontinue the aspirin and clopidogrel.

The following day the patient developed hematochezia, hypotension and anemia requiring a transfusion of 3 units of packed red blood cells to maintain a hemoglobin over 10 g/dL. A second urgent EGD showed evidence of ac-

tive bleeding at the sphincterotomy site, and electrocautery and epinephrine injection were applied for hemostasis.

Over the next 24 hours the patient continued to have multiple maroon stools and a third EGD was performed. Prior to the procedure, the patient was counseled on the risks of cyanoacrylate and its off label usage and agreed to proceed. During the procedure, a large adherent clot was removed with a snare to reveal a pulsating arterial bleed from the sphincterotomy site. Using a Marcon-Haber needle, 1 cc of cyanoacrylate was injected inside the vessel. There was immediate hemostasis. The patient tolerated the procedure well, without clinical evidence of further gastrointestinal bleeding.

**Conclusion:** Post-sphincterotomy hemorrhage has an incidence of approximately 2%. In this case, traditional endoscopic methods failed to achieve lasting hemostasis, likely due to the concomitant use of aspirin and clopidogrel.

Cyanoacrylates are a class of tissue adhesives that solidify upon contact with weak bases such as water and blood. Cyanoacrylate application is increasingly used as an alternative means of achieving hemostasis when traditional endoscopic methods have failed, though it is not FDA approved for this indication. To the best of our knowledge, this is the first report of the successful use of cyanoacrylate to achieve hemostasis in post-sphincterotomy bleeding.

1108

### Combined Endoscopic Assisted Laparoscopic Resection of Upper and Lower Gastrointestinal Adenomas, Carcinoids, and Stromal Tumors – An Effective and More Targeted Resection of GI Tract Lesions

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**Purpose:** Endoluminal screening and surveillance have led to the identification of both symptomatic and clinically silent mucosal and nonmucosal lesions throughout the gastrointestinal tract. A key challenge is to remove these lesions while minimizing the extent and morbidity of resection. The purpose of this study is to demonstrate the safety and utility of combined endoscopic-laparoscopic resection of a variety of lesions from the gastrointestinal tract.

**Methods:** We present a series of nine patients with gastrointestinal polyps and nodules in the stomach, duodenum, and colon. Laparoscopic ports were inserted, the abdomen insufflated, and the stomach, duodenum, or colon was mobilized. During simultaneous intraoperative endoscopy, lesions were transilluminated and mobilized with biopsy forceps, and compressed laparoscopically from the serosa to confirm position. For some lesions, a suture was passed from serosa to mucosa, and resection performed with an endo-stapler.

**Results:** Five lesions were located in the upper GI tract and four in the colon. Upper GI tract lesions included a 3.5 cm flat mucosal duodenal adenoma, a gastric antral neuroendocrine tumor, and a 2 cm antral gastrointestinal stromal tumor (GIST). Colonic lesions included a 4 cm cecal villous adenoma, transverse and right colonic tubular and tubulovillous adenomas, and a serrated adenoma. Resection specimens demonstrated complete removal of all lesions. Mean procedure time was  $159.7 \pm 56.9$  min (range 60–268 min), with upper GI tract shorter than colonic lesion resections (mean  $133 \pm 51.4$  min vs  $181 \pm 56.8$  min). Patients were discharged from hospital after a mean  $4.88 \pm 2.1$  d (range 2–7 d), similar for upper ( $5 \pm 1.41$  d) and lower ( $4.8 \pm 1.6$  d) GI tract lesions.

**Conclusion:** Combined endoscopic-laparoscopic resection of gastrointestinal polyps is straightforward, well-tolerated with a post-procedure length of stay of 4.9 days, and without significant adverse events. This series highlights the safety and efficacy of this approach, which will aid in the targeted management of a variety of mucosal and nonmucosal lesions throughout the GI tract, with improved lesion identification, short procedural and recovery times, excellent tolerability, and the avoidance of more extensive surgical resection.

1109

**ERCP Training: Too Little, Too Late and Too Lax**

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**Purpose:** There has been much debate over ERCP training during a 3-year gastroenterology (GI) fellowship. Our study is the first to survey gastroenterologists who have completed fellowship and assess their experiences training in ERCP.

**Methods:** Using an Internet survey tool, we developed a survey which was emailed to gastroenterologists in the Midwest.

**Results:** 62 gastroenterologists completed the survey (N = 62). 37% (23/62) described their practice as academic, 32% (20/62) as single-specialty, 18% (11/62) as multi-specialty, and 13% (8/62) as solo or primary care. 94% (58/62) did a 2–3 year fellowship and 6% (4/62) did fellowship in 4–5 years. 5% (3/62) did an additional 1-year fellowship in ERCP. The median number of ERCPs done during fellowship was 25–50. 14.5% (9/62) felt very well trained, 6.5% (4/62) felt well trained, 40% (25/62) felt somewhat well trained, and 39% (24/62) did not feel well trained at all in ERCP during fellowship. After fellowship, 49% (28/57) were granted full privileges, 5% (3/57) diagnostic but restricted therapeutic, 4% (2/57) diagnostic only, 7% (4/57) granted with supervision, and 5% (3/57) were denied privileges in ERCP. 30% (17/57) did not ask for privileges. 63% (39/62) are performing ERCP after fellowship and 37% (23/62) are not. 29% (18/62) pursued additional training after fellowship, while 71% (44/62) did not. Of those who had more training, 61% (11/18) were trained by their partners, 22% (4/18) by an ASGE course, and 17% (3/18) from another source.

**Conclusion:** Traditional 3-year GI fellowships do not provide adequate training for ERCP. The median number of ERCPs completed during fellowship in this cohort was 25–50, which is well below the current consensus of 180–200 needed for ERCP competency. Despite this, 49% were granted full privileges. The majority of those who pursued additional training in ERCP after fellowship were trained by their partners, while some trained through the ASGE or other sources. None of these methods provide formal evaluation or ACGME oversight. Furthermore, training and privileging from partners is biased. ERCP privileges should no longer be granted to fellows completing a 3-year fellowship but rather reserved for those who complete a 4th year formal pancreato-biliary training program.

1110

**Is ERCP Necessary for Removal of Biliary Stent?**

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**Purpose:** ERCPs are routinely done to remove biliary stents. From a technical, cost and patient safety and comfort perspective an EGD may suffice

to remove biliary stents. However, therapeutic interventions requiring an ERCP may preclude this option. Thus, the aim of this study was to determine the frequency of endoscopic therapy during ERCP for biliary stent removal.

**Methods:** Procedure notes for ERCP for stent removal performed from January 2005 to December 2006 were retrieved. 109 cases were identified. Cases with initial ERCP done at another institution, pancreatic stent exchange or removal and duplicate procedures were discarded. Patient demographics and ERCP therapies on initial and repeat ERCP were analyzed.

**Results:** A total of 69 patients were analyzed. On repeat ERCP 59% required endoscopic therapy. 47% of patients with benign pathology during the initial ERCP required therapy on repeat ERCP. Groups were further divided by the results on initial ERCP into choledocholithiasis (52% therapy on repeat ERCP), benign obstruction (55% repeat therapy), malignancy (100% repeat therapy), and biliary leak (13% repeat therapy). Mean duration between ERCPs in the biliary leak group with normal result on repeat ERCP was 80 days (range 35–168). One person with a biliary leak on repeat ERCP underwent procedure 37 days after the initial ERCP.

**Conclusion:** A high incidence of abnormal findings requiring interventions on repeat ERCP even in benign conditions precludes the use of EGD for stent removal without ERCP. Patients who underwent ERCP for biliary leak might be good candidates for EGD. However, a larger study in this cohort is necessary to reach this conclusion.

1111

**Critical Evaluation of the Efficacy of 4 Different Colon Preparations**

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**Purpose:** The aim of this study is to evaluate the efficacy of various bowel preparations in accomplishing colonic cleansing for optimal mucosal visualization during colonoscopy.

**Methods:** The study included a cohort of 980 patients who underwent colonoscopy at endoscopy center in last 3 years. Study patients were divided into 4 groups of 245 each receiving a different type of bowel preparation as shown in table 1.

A Colon Prep Score (CPS) was devised to compare the quality of the different bowel preparations used.

The colonoscopy results from all patients were statistically analyzed using one-way ANOVA and expressed as mean  $\pm$  1 SD.

**Results:** Group I patients had a mean CPS  $\pm$  1 SD of  $3.11 \pm 0.91$ . Group II patients achieved a CPS of  $3.37 \pm 1.16$ . The patients in group III actually showed the highest mean CPS of  $3.44 \pm 1.12$ . Group IV patients reached a mean CPS of  $3.23 \pm 1.01$ . Group III patients demonstrated a statistically

Result on Initial ERCP

	Choledocholithiasis/ Microlithiasis (N = 25)	Benign Obstruction/ Stricture (N = 20)	Malignant Obstruction (N = 16)	Biliary Leak (N = 8)	Benign Pathology (N = 53)	Total (N = 69)
Demographics						
Mean Age, y	57	65	66	40	58	60
Men, n (%)	10 (40)	7 (35)	9 (56)	4 (50)	21 (40)	30 (43)
Mean Days between ERCPs	59	69	74	75	65	67
Normal Result on Repeat ERCP, n (%)	9 (36)	5 (25)	0	7 (88)	21 (40)	21 (30)
Therapy on Repeat ERCP, n (%)						
Dilation/Balloon Extraction/Lithotripsy	11 (44)	9 (45)	2 (13)	0	20 (38)	22 (32)
Sphincterotomy	6 (24)	2 (10)	4 (25)	0	8 (15)	12 (17)
Stent Placement*	4 (16)	6 (30)	16 (100)	1 (13)	11 (21)	27 (39)
Any Therapy*	13 (52)	11 (55)	16 (100)	1 (13)	25 (47)	41 (59)

\*P &lt; 0.01

higher CPS ( $P < 0.0006$ ) in colon cleansing as compared to group I patients. Similarly, group II patients also showed improved colon cleansing statistically ( $P < 0.006$ ) as compared to group I patients.

**Table 1.** Study Groups

Group	Number of Patients	Colon Preparation Used
I	245	Magnesium citrate and dulcolax
II	245	Oral Sodium phosphate (Fleets), Dulcolax and Powder PEG-3350 in dosage of 136 g
III	245	Powder PEG-3350 in dosage of 204 g
IV	245	Oral Sodium phosphate (Fleets), Dulcolax

**Table 2.** Colon Prep Score (CPS)

Grades	Score	Description
A	4	A completely clean colon with no stool and little or no liquid residue.
B	3	A moderately clean colon with small pools of liquid residue but no solid stool.
C	2	A fair prep with large pools of liquid residue or solid stool sticking to the colon wall but no solid stool in the lumen.
D	1	A poor prep with large amounts of liquid residue and some solid stool, but study completed.
F	0	A failed prep due to large amounts of solid, liquid stool preventing the complete examination of the colon.

**Conclusion:** Overall, all four colon preparations achieved an average CPS greater than 3.0 indicating clinically adequate colonic cleansing. However, powder PEG-3350 alone and in combination with oral sodium phosphate was observed to be statistically superior to magnesium citrate when used for colon preparation for colonoscopy.

## 1112

### Utility of Endoscopy in Evaluating Abnormal Findings of the Gastrointestinal Tract on CT Scan

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**Purpose:** Abdominal CT scans are frequently performed for a variety of abdominal complaints. Not infrequently changes are noted of the gastrointestinal tract on these radiographic studies which prompts further endoscopic evaluation. It is unclear whether the cost and risks of endoscopy are justified given the subsequent yield on endoscopic examination of changes seen on abdominal CT scans. Thus, the aim of this study was to correlate endoscopic findings with abdominal CT scan findings that prompted the subsequent endoscopic procedure.

**Methods:** This retrospective study was undertaken after appropriate IRB exemption was obtained. Medical records of 169 patients referred for endoscopy following abnormal CT scan findings were reviewed from July 1,

2005 to June 30, 2006. Patient demographic information as well as findings of the CT scan and endoscopic procedures was reviewed.

**Results:** The average age of patients ranged from 18 to 89 with a mean of 55, 41% of these patients were male and 59% were female. The most common pre-radiographic chief complaint was abdominal pain (66%). An abnormal abdominal exam was noted in only 34% of patients on physical exam. CT scan changes were noted less commonly of the upper GI tract (45/169 patients) than in the lower GI tract (124/169 patients). Radiographic changes of the upper GI tract was thickening of the esophagus, stomach, or duodenum in 39/45 patients. Only 25 of these 39 patients on endoscopy had pathology which consisted of ulceration or inflammation in the respective organs. Thus, positive predictive value of thickening of the upper GI tract seen on abdominal CT scan was 64% at the time of endoscopy. Of the 124 patients with pathology in the lower GI tract noted on CT scan, the most common finding once again was wall thickening in 109/124 patients. Only 36 of the 109 patients were found to have pathology on endoscopic exam. Inflammation was the most common result of the colonoscopy followed by hyperplastic polyp. Thus, the positive predictive value for thickening seen of the lower GI tract on abdominal CT scan was 33%.

**Conclusion:** Thickening of the gastrointestinal tract is not uncommonly noted on abdominal CT scans. The resultant endoscopic evaluations of these changes appear to yield more findings when changes are seen in the upper GI tract as compared to the lower GI tract. Thus, while the gold standard endoscopic examination is warranted to follow up abnormal CT scan findings it is especially important when these changes pertain to the upper GI tract.

## 1113

### Socioeconomic Status Directly Affects the Probability of Percutaneous Endoscopic Gastrostomy Placement

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**Purpose:** The decision to place a percutaneous endoscopic gastrostomy (PEG) tube is often a difficult one due to limited data on the survival benefit in patients with multiple comorbidities. Many studies have aimed to identify risk factors of poor outcome after PEG placement, but few have aimed to identify factors affecting the likelihood of PEG placement. We hypothesized that PEG tube insertion is inversely correlated to the patient's socioeconomic stratum (SES).

**Methods:** We compared the number of PEG tubes placed per total procedures in endoscopy departments in three area hospitals throughout the 2003 and 2006 calendar years. These hospitals reside in distinctly different socioeconomic areas. The average adjusted gross median income was verified by the zip code of the hospital from the 2000 US Census.

**Results:** Distinct SES of the three area hospitals were verified by the 2000 US Census at \$29,526, \$51,802, and \$77,538 for low, medium, and high SES, respectively. In 2003, there were 6.2%, 2.2%, and 1.5% PEGs placed in the low, medium, and high SES hospitals, respectively. In 2006, there were 6.6%, 3.9%, and 0.01% PEGs placed in low, medium, and high SES hospitals, respectively. These data reveal a trend of increasing number of PEG tubes placed with decreasing SES which persists from 2003 to 2006.

**Conclusion:** There are several possible explanations for this inverse correlation between PEG placement and SES. First of all, lower SES patients may avoid routine health care and present with more advanced medical conditions. Second, lower SES patients may have distant family members who will

### Socioeconomic Strata and PEG Placement Results

Socio-Economic Stratum	200 Census Median Income	Total # PEG (2003)	Total # Procedures (2003)	%	Total # PEGs (2006)	Total # Procedures (2006)	%
Low	\$29,526	456	7,312	6.2%	466	7,083	6.6%
Middle	\$51,802	223	10,049	2.2%	246	6,291	3.9%
High	\$77,538	394	25,552	1.5%	195	20,951	0.01%

elect maximal treatment after long separations. Third, higher SES patients may have more involved families who know their wishes, which often is to withhold invasive procedures. Finally, there is a tendency towards increased nursing home placements for patients in lower SES areas whose families cannot hire specialized care. Nursing homes often require PEG placement prior to admission for patients with poor oral intake. In conclusion, PEG tube placement increases as SES decreases.

## 1114

# **Prokinetics Infusion Prior to Endoscopy for Acute Upper Gastrointestinal Bleeding: A Randomized, Controlled, Double-Blind & Placebo-Controlled Trial**

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**Purpose:** We investigated the relative benefit in the use of erythromycin/metochlopramide to improve visualisation before endoscopy in acute GI bleeding, assisted by subjective & objective criteria.

**Methods:** Forty-five patients with hematemesis were randomly assigned to receive placebo (intravenous saline), intravenous metochlopramide or intravenous erythromycin before endoscopy in a double-blind study. All the patients had gastric lavage done prior to the infusion of the study medicine/placebo. The study had 15 patients in each arm and randomization was done by the Department of Pharmacy.

**Results:** Characteristics of patients at admission were similar in the three groups. Nineteen patients (42%) had peptic ulcer disease & nine patients (20%) had esophageal varices. The gastric mucosa was entirely visualized by the endoscopist in 86% of patients in the erythromycin group, versus 66% in the metochlopramide and placebo groups ( $P > 0.05$ ). The quality of examination of the upper gastrointestinal tract, assessed by using a four-point scoring system (from zero to 3 with zero as the worst and three as the best) was better in the erythromycin group (2.53/3) compared to metochlopramide (2/3) and placebo (2.2/3) with ( $P > 0.05$ ). Clots were found in the stomach in 13% of the patients in the erythromycin group compared to 33% in the metochlopramide and the placebo group. Repeat endoscopy was needed in one patient in the erythromycin group and three patients in the placebo and metochlopramide group. The mean length of hospital stay was not different among the three groups. The mean amount of blood transfusion needed was 2.26 in the erythromycin group, 2.86 in the placebo group and 3.66 in the metochlopramide group. All patients tolerated erythromycin and metochlopramide with no adverse effects.

**Conclusion:** The study did not detect a significant difference between placebo and either study medication. There is a possibility of a type II error because of a relatively small sample size and high rate of success in the placebo arm.

We estimated that, given the placebo response rate, about 100 patients needed to be enrolled in each arm to have a 90 percent chance of detecting a statistically significant ( $P$  value  $< 0.05$ ) difference in the medications.

The study also suggests that a thorough lavage with normal saline may adequately cleanse the upper GI tract for good visualization in acute upper GI bleeding.

## 1115

# **Presence of Lymph Node Vasculature: A New EUS Criterion for Benign Nodes?**

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**Purpose:** Since lymph nodes normally have prominent centrally located blood vessels which may become obliterated with tumor infiltration, the presence of vasculature traversing through a lymph node has been noted to coincide with benign cytology. We sought to determine the test characteristics

of the presence of intranodal mediastinal vasculature during endoscopic ultrasound (EUS) as well as to reexamine the classic indicators of malignancy.

**Methods:** 67 mediastinal lymph nodes were evaluated by EUS in 66 patients over a 1-year period. We evaluated for the four classic features of malignant nodes as well as for the new characteristic in question. Vasculature was considered benign when it traversed through the center of the lymph node without disruption and had normal doppler flow.

**Results:** Of the 67 lymph nodes evaluated, 29 (43%) were found to be malignant on cytopathologic review. Benign vascular markings were present in 15 of the 67 (22.4%) lymph nodes evaluated. All 15 (100%) of these nodes were found to have benign FNA results. Lack of benign vasculature was found to have a positive predictive value of 55.8% while the presence of benign vasculature had a negative predictive value of 100%. Adding a fifth feature to the present diagnostic criteria for characterizing lymph nodes by EUS increased the sensitivity of determining malignant nodes.

**Conclusion:** We found that when benign vasculature was seen, it was universally associated with a benign lymph node. The addition of this EUS finding improves the ability to characterize lymph nodes and predict the likelihood of malignant involvement.

## 1116

# **Colonic, Non-Rectal, Submucosal Lesions Referred for EUS**

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**Purpose:** EUS-FNA is commonly used to evaluate submucosal lesions of the colon and rectum. Rectal lesions, being more common and accessible, have been better characterized. The objective of our study is to retrospectively review all submucosal, non-rectal, colonic lesions referred to a tertiary care center for EUS examination.

**Methods:** All patients referred to the University of Maryland for EUS evaluation of a colonic, non-rectal, submucosal lesion between 9/02 and 5/07 were included. Patient demographics collected included age, sex, and date of procedure. Procedure related data collected included location of the lesion, echoendoscope used, sonographic characteristics (i.e. intraluminal vs. extraluminal, wall layer of origin, echotexture), biopsy techniques used, and biopsy results.

**Results:** A total of 29 patients were referred for evaluation of 31 submucosal lesions in the colon (non-rectum). The mean age was 59 (62.1% female). Right-sided lesions (74.2%) outnumbered left-sided lesions (25.8%). Three lesions were diagnosed by endoscopic appearance alone and therefore EUS was not performed (2 lipomas, 1 external compression). Twenty-eight lesions were examined by EUS. A miniprobe was used in 92.9%. The 12 MHz (UM-2R) miniprobe was used in 57.1%, the 20 MHz (UM-3R) miniprobe in 35.7%. A radial echoendoscope (GF-UM160) was used in 7.1% and a linear echoendoscope (GF-UCT140, GF-UC140) in 10.7% of cases.

Twelve out of the 28 (42.9%) lesions were hyperechoic on EUS and diagnosed as lipomas. One isoechoic lesion was removed by endoscopic mucosal resection and proved also to be a lipoma. Two anechoic lesions (7.1%) were thought to represent simple cysts. Seven lesions (25%) were hypoechoic on EUS. In this group, two adenocarcinomas (both diagnosed by FNA), one lymphoma (diagnosed by bite on bite biopsies and FNA), and one endometrioma (diagnosed by FNA) were found. Attempts to sample two of the hypoechoic lesions using bite on bite biopsies revealed only normal mucosa. Three "lesions" were found to be inverted appendices (10.7%). One study revealed mild external compression in a normal cecum. One exam of a "prominent fold" revealed mildly thickened mucosa on EUS. Mucosal biopsy revealed adenoma.

**Conclusion:** Colonic, non-rectal, submucosal lesions are uncommon. Most can be diagnosed with confidence by endoscopic appearance and miniprobe endosonography. Lipomas represent the most common finding. Hypoechoic lesions may represent malignancy and warrant tissue sampling.

1117

### Endoscopic Full-Thickness Suturing in the Management of Gastric Wall Defects

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**Purpose:** The Plicator<sup>TM</sup> (NDO Surgical, Inc.) is an endoscopic device developed for the treatment of GERD based on the principles of anti-reflux surgery. The procedure places a transmural full-thickness suture under direct endoscopic visualization. Endoscopic full-thickness plication permits rapid and easy placement of transmural sutures and might be useful as an endoscopic alternative to surgical intervention in patients with GI wall defects.

**Methods:** By means of the Plicator device, a pre-tied suture can be deployed to create a serosa-to-serosa full-thickness fold of GI-tissue. The average procedure takes about 10–20 minutes to perform and provides placement of a durable transmural suture comparable to a surgical suture. Therefore, we investigated the possible use of the Plicator device for endoscopic restoration of GI wall defects. Four subjects received endoscopic full-thickness suturing for restoration of GI wall defects. Written informed consent was obtained by all patients before intervention. Three received endoscopic full-thickness suturing post or during endoscopic mucosal resection (EMR). One subject received endoscopic full-thickness plication for treatment of a fistula.

**Results:** Mean procedure time for endoscopic full-thickness plication was 15 minutes. All Plicator interventions were performed under propofol and midazolam sedation. In all cases, GI wall patency could be restored. All post-procedure endoscopic and X-ray follow-up investigations confirmed complete GI patency. No procedure-related complications occurred during or after any of the full-thickness suturing interventions. Reestablishment of enteral feeding was uncomplicated in all presented cases. No modification of the standard Plicator instrument or sutures were necessary for endoscopic full-thickness suturing in the presented cases.

**Conclusion:** The endoscopic full-thickness Plicator permits rapid and easy placement of transmural sutures. Restoration of gastric wall defects was easy to accomplish in all presented cases. If surgical intervention seems necessary, a Plicator suture seems an appropriate endoscopic alternative technique. Clipping should remain the first choice in small defects and the Plicator intervention should be limited to cases with larger defects that might otherwise require surgical intervention.

1118

### Endoscopic Mucosal Ablation for the Treatment of Gastric Antral Vascular Ectasia (GAVE) Using the HALO<sup>90</sup> System: A Pilot Study

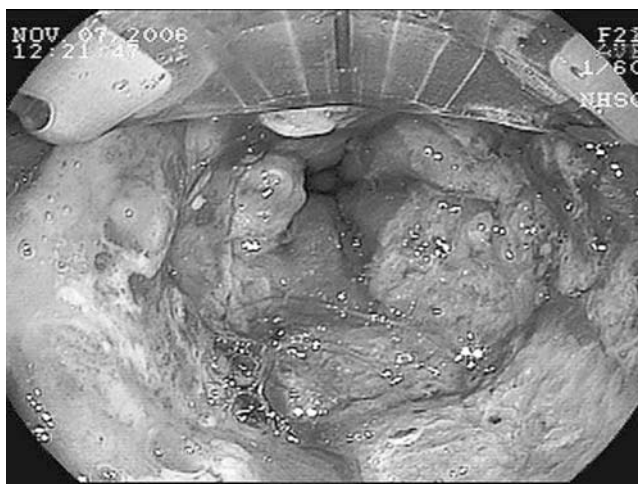
Seth A. Gross, MD, Mohammad Al-Haddad, MD, Kanwar R.S. Gill, MD, Anthony N. Schore, MD, Michael B. Wallace, MD\*. Gastroenterology and Hepatology, Mayo Clinic, Jacksonville, FL and Gastroenterology and Hepatology, Indiana University, Indianapolis, IN.

**Purpose:** Gastric antral vascular ectasia (GAVE) often results in gastrointestinal bleeding and chronic anemia. Treatment options are limited and include medical, endoscopic, and surgical therapies. The aim of our study was to assess the utility of endoscopic mucosal ablative therapy using radiofrequency, HALO<sup>90</sup>, system for patients with GAVE refractory to other therapies.

**Methods:** A prospective pilot study analyzing our first 6 consecutive patients who received treatment with this ablative device for GAVE. Patients had endoscopic confirmation of GAVE and correlation of the disorder with chronic bleeding and transfusion dependency. All patients had failed prior endoscopic therapy with other techniques. Halo<sup>90</sup> ablation was repeated circumferentially around the antrum until all areas of GAVE were treated (Fig. 1). Clinical parameters evaluated included hemoglobin, blood transfusion frequency and volume, GAVE extent, and number of ablation sessions needed to reach a primary endpoint.

**Results:** Six patients, four males and two females (mean age 58, range 47–65) underwent ten sessions of endoscopic mucosal ablation of antral lesions (mean procedure time 29 min, mean number of sessions 1.7, range 1–3). Mean hemoglobin improved from 8.6 to 10.2 g/dl after treatment. Five of 6 patients are no longer dependent on blood transfusion to maintain a stable hemoglobin. There were no complications.

**Conclusion:** This pilot study suggests that endoscopic mucosal ablation using the HALO<sup>90</sup> system should be considered as part of the armamentarium for the treatment of refractory GAVE. To further validate the clinical benefit of this technique, we recommend prospectively evaluating this intervention in larger trials and in comparison to other established therapies, such as APC.[figure1]



1119

### Learning Curve for Double-Balloon Enteroscopy (DBE) at a U.S. Center

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**Purpose:** Reports of DBE experience demonstrate the positive influence of DBE on management of small intestine disorders, but also note long procedure time, the use of special training, and a learning curve when endoscopists first perform DBE. Our aim was to examine the learning curve for a single endoscopist's initial experience with DBE.

**Methods:** We analyzed the first 250 DBE performed at our center (9/05 – 4/07). DBE were performed by a single endoscopist using the Fujinon EN-450T5 and P5 enteroscopes. Complications, procedure duration, length of small intestine examined, fluoroscopy time, rate of total enteroscopy, and proportion of DBE judged clinically "Helpful" were analyzed for sequential groups of 50 DBE, with comparison to the first 50 procedures.

**Results:** The only major complication was a self-contained perforation in a patient in the last group of 50 DBE. Procedure parameters for sequential groups of 50 DBE are shown in Tables 1 and 2; the statistic (p) compares each group of 50 DBE to the first group.

**Conclusion:** There was no statistical decrease of DBE duration or fluoroscopy time with increasing experience. For oral DBE, the length of intestine examined did not increase with experience for up to 250 procedures, and increased for anal DBE after 100 DBE. The rate of total enteroscopy, and proportion of "Helpful" procedures increased after 150 DBE. An endoscopist may be able to perform safe and useful DBE after limited training, expertise may require more than 100 to 150 procedures.

**Table 1.**

Position in DBE Series	n	DBE Duration (min) Mean $\pm$ SD	P	Length examined (cm) mean $\pm$ SD	P	Fluoroscopy time (min) mean $\pm$ SD	P
<b>Oral</b>							
1–50	28	96 $\pm$ 24	—	220 $\pm$ 86	—	4.6 $\pm$ 2.3	—
51–100	23	108 $\pm$ 38	.42	229 $\pm$ 52	.62	4.5 $\pm$ 1.7	.98
101–150	31	100 $\pm$ 32	.78	226 $\pm$ 95	.92	5.0 $\pm$ 2.4	.49
151–200	33	98 $\pm$ 42	.78	207 $\pm$ 78	.33	4.0 $\pm$ 1.7	.46
201–250	30	107 $\pm$ 23	.04	236 $\pm$ 81	.43	5.0 $\pm$ 1.9	.29
<b>Anal</b>							
1–50	22	97 $\pm$ 40	—	101 $\pm$ 53	—	5.1 $\pm$ 4.0	—
51–100	27	103 $\pm$ 31	.56	120 $\pm$ 43	.09	6.6 $\pm$ 3.7	.11
101–150	19	94 $\pm$ 38	.88	148 $\pm$ 68	.01	5.6 $\pm$ 2.9	.28
151–200	17	84 $\pm$ 18	.29	132 $\pm$ 77	.14	3.9 $\pm$ 2.0	.49
201–250	20	82 $\pm$ 37	.15	122 $\pm$ 81	.53	4.0 $\pm$ 2.3	.72

**Table 2.**

Position in DBE Series	Successful Total Enteroscopy	P	% Clinically “Helpful”	P
1–50	8% (1 of 13)	—	58%	—
51–100	8% (1 of 12)	1	70%	.45
101–150	17% (2 of 12)	.59	73%	.31
151–200	63% (5 of 8)	.01	86%	.017
201–250	67% (10 of 15)	.002	89%	.0006

**1120****Do “No-Shows” Share Common Characteristics?**

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**Purpose:** Failure to keep scheduled endoscopy appointments (No-shows) is common. This may adversely affect the health of no-show patients. It is also an inefficient use of staffing and considerable losses of health-care revenue. Our aim was to examine whether no-show patients share similar and identifiable characteristics

**Methods:** Data were collected, during 10 weeks in Spring '07, from patient records and telephone interviews (for all procedures) of two staff gastroenterologists in our hospital.

Data on age, sex, race, type of procedure, indication, means of transport, time of day, and day of week of appointment, history of past no-shows, education and employment were collected

**Results:** A total of 623 endoscopies were scheduled [30% EGD, 60% colonoscopy, 10% both]; mean age  $57 \pm 14$ (sd) yrs; 69% [females]; 40% Hispanic, 40% African American, 20% Whites. No-shows were 17% ( $N = 105$ ). No difference in age ( $P = .834$ ), sex ( $P = .842$ ), type of procedure ( $P = .253$ ) or race ( $P = .126$ ) between both groups. But several patterns distinguished patients who showed from no-shows. No-shows were twice as likely on Mondays and Fridays ( $P = .002$ ). In colonoscopies, 1.5 times more no-shows were seen in males than females ( $P = .046$ ). No-shows were 5.5 times more likely in morning ( $P < .0005$ ). No-shows also were 1.5 times more likely among Hispanics vs. Whites and African Americans ( $P = .025$ ). Hispanics were 1.4 times and 1.6 times more likely to provide incorrect contact information than African Americans and Whites ( $P = .003$ ), respectively. The major reasons given for No-show were 1) Correctable causes [no one to accompany /drive (17%), unable to take prep (15%), fear of procedure (5%)] 2) Non-correctable causes [sickness (20%), no time off work (7%), vacation/ travel (3%)].

Finally, 62% of Hispanics, 31% of African Americans and 7% of Whites provided incorrect contact information halting the 48-hr pre-appointment reminder phone calls

**Conclusion:** These findings suggest some general characteristics in Bronx, NY residents; 1) No-shows are more common in Hispanics 2) Males are more likely to be no-shows 3) No-shows are more prevalent on Mondays and Fridays 4) No-shows cause significant waste of human resources and healthcare funds 5) Majority of patients who did not show up fell in the correctable group We feel this information should be considered in scheduling endoscopic procedures.

Other measures such as updating contact information, reminder calls and clarifying patients concerns would help. We also feel free transportation could be useful.

**1121****The Study of Associated Cellular DNA Damage in Proliferous Cells by Vital Dyes at Concentrations Used in Clinical Chromoendoscopy**

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**Purpose:** Chromoendoscopy, aided by the use of vital dyes, has been shown to improve the identification of mucosal abnormalities. Although it is widely assumed that the vital dyes are safe at the concentration of clinical application, their iatrogenic damage, especially on proliferous cells, has rarely been investigated.

**Methods:** Here, we selected methylene blue (MB) and indigo carmine (IC), two wide used vital dyes in chromoendoscopy, to study their effects on cell damage and the mechanisms involved. To simulate chromoendoscopy in vitro, methylene blue or indigo carmine dye was added to primary cells isolated from patients biopsy and mesenchymal stem cells (MSC) before they were exposed to cold white light for 3–30 min. The alkaline comet assay was used to determine cell DNA damage. Two indexes were choiced, i.e. amount of DNA in the comet tail and OliveTailMoment. Apoptosis of the cells was determined by flow cytometry analysis using Annexin V-FITC/PI staining. DCFH-DA (dichlorofluorescein diacetate) probe was used to determine endocellular Reactive Oxygen Species (ROS).

**Results:** The levels of DNA damage in primary cells isolated from patients biopsy and MSC treated with methylene blue in the light were significantly increased compared to that of control cells treated with white light alone or indigo carmine either in the light or in the dark, or with methylene blue in the dark. The DNA damage levels were related to the length of light exposure, and the damage was recovered to a certain level after light withdraw. The DNA impairment was associated with increase of apoptosis and endocellular ROS. The similar results were observed in BGC823 and SGC7901 adenocarcinoma cells in our previous study although there was some difference.



**Conclusion:** Our study demonstrated that MB, but not IC induced DNA damage and apoptosis of the target cells through stimulating production of ROS when used as a dye during chromoendoscopy. Because of the association between oxidative DNA damage, mutagenesis and the development of malignancy, especially for proliferous cells, it should be caution to use MB in chromoendoscopy in high-risk groups. Vital dyes are not always safe, and many other dyes should be evaluated carefully.

## 1122

### Endoscopy after Myocardial Infarction: A Retrospective Evaluation of Safety from a Tertiary-Care Center

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**Purpose:** Myocardial infarction (MI) and gastrointestinal (GI) bleeding are often related co-morbidities. Patients with anemia due to GI bleeding are at increased risk of MI while patients with MI on potent anticoagulants may exacerbate GI bleeding. Both conditions have many complications, especially with procedures. The risk of endoscopy after myocardial infarction has been postulated, but studies vary in definitions and methods and have not used troponin I as selection criteria. This study examined the effect of EGD after MI at a tertiary-care center.

**Methods:** A retrospective study (1/01–8/06) of 63 patients who underwent EGD within 30 days of a MI at a single tertiary-care center. Patients were identified by ICD-9 codes for MI (STEMI & NSTEMI) and CPT codes for EGD. An extensive chart review was performed. MI was defined as troponin I greater than laboratory reference “diagnostic of MI.” Data was extracted for type of MI, peak troponin I, time from MI to EGD, Apache II score at EGD, cardiac catheterization prior to EGD, and medical complications within 24 hours of EGD. Medical complications were defined as any documented changes in patients’ symptoms, vital signs (BP < 90/60 or > 180/100 mmHg, HR > 100 or < 60 bpm, RR > 24/minute, O<sub>2</sub> saturation < 90%, temperature < 35.0°C), and telemetry (ventricular or atrial arrhythmias). The data was analyzed by the chi-square test and Fisher’s exact test.

**Results:** Sixty-three patients met the search criteria. Mean peak pre-catheterization troponin I was  $24.3 \pm 67.2$  ng/mL. Mean time from MI to endoscopy was  $5.8 \pm 6.2$  days. Mean Apache II score was  $13.0 \pm 5.4$ . Complications were identified in 29.5%. Complications consisted of hypotension (6), hypertension (2), tachypnea (2), sinus tachycardia (3), sinus bradycardia (1), PVCs (1), hypothermia (1), and chest pain (2). Cardiac catheterization was performed in 22.6% of patients prior to endoscopy. STEMI patients underwent EGD sooner than NSTEMI patients ( $P = 0.0499$ ). Otherwise, no significant differences were noted between types of MI and cardiac catheterization status for peak troponin I, Apache II score, or complications.

**Conclusion:** EGD after acute MI appears to be relatively safe. Although the occurrence of complications were 29.5%, these complications were only minor and not associated with mortality. Complications after EGD may be attributed to the EGD, overall health status of the patient, or combination of both.

## 1123

### New Suction-Aid Bite Block Enables Continuous, Hands-Free Suction and Provides Greatly Improved Patient Comfort and Procedure Efficiency

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**Purpose:** Recent advancements in gastroenterology have led to increasingly complex and lengthy diagnostic and therapeutic procedures involving the

upper gastrointestinal tract. Frequent suctioning of the mouth is needed to remove oral secretions and prevent aspiration. The suctioning is usually done by the endoscopy assistant who also performs other functions. The suction catheter needs to be physically held in place by the assistant, causing delays in performing biopsies or procedures to control gastrointestinal hemorrhage.

**Methods:** We developed Suction Aid bite block with several modifications to the traditional bite block.

**Results:** Our bite block features multiple openings to allow stable positioning of various sizes of suction catheters, which remain in a fixed position in the mouth, thereby allowing continuous hands-free suction. This eliminates the need for the endoscopy assistant to hold on to the suction catheter. With continuous hands-free suction, patient monitoring and comfort are improved. The endoscopist and endoscopy assistant can focus on timely completion of the diagnostic or therapeutic procedure. This patent pending device has been successfully utilized in various upper endoscopic procedures such as EGD, EUS, ERCP, PEG placement, and small bowel enteroscopy.

**Conclusion:** Our new Suction Aid bite block designed for use in any upper gastrointestinal endoscopy procedure and can accommodate various commonly used suction cannulae. It will improve patient comfort and help the endoscopist and endoscopy assistant in managing efficiency of the procedure.

## 1124

### Management of the Poorly Prepared Colonoscopy Patient:

#### Colonoscopic Colon Enemas as a Preparation for Colonoscopy

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**Purpose:** Colonoscopic colon enema (CCE) is an option for the management of patients who are suboptimally prepared for colonoscopic examination due to retained fecal material.

**Methods:** After colonoscopy is performed and the colonoscopist has reached the right colon and the colon is deemed to be inadequately prepared, the contents of two commercially available bisacodyl enemas are combined and

Patient Data	
Gender	
Male	13
Female	13
Age	
Range	26–90
Mean	64.1
Median	65
Primary Prep	
RVPB*	13
RVPB enhanced	2
PIE**	5
Other	4
None	2
CCE placed in	
Cecum	18
Asc. colon	5
Trans. colon	2
Desc. colon	1
Diagnoses	
Normal	13
Polyps	6
Diverticulosis	4
Fecal impaction	1
Rectal prolapse	1
Colovaginal fistula	1
Rectosigmoid CA	1

\* Reduced volume PEG + bisacodyl, \*\* Pulsed Irrigation Evacuation

instilled into the right colon and another into the midsigmoid colon via the colonoscope biopsy channel. Patients are allowed to recover from propofol sedation, expel the luminal contents, resedated, and examined.

**Results:** In this fashion, 26 patients over a 25 month period were successfully cleansed of their retained fecal contents, permitting satisfactory colonoscopic examinations. This avoided the need for postponement of the procedure.

**Conclusion:** CCE is an innovative and simple option available to the colonoscopist to manage the patient with an inadequately prepared colon. Since it requires only minimal patient participation, it is also useful for patients who are unable or unwilling to undergo an ordinary colonoscopy preparation.

## 1125

### Accuracy of Endoscopic Ultrasound in Diagnosing Mediastinal Nodal Staging of Esophageal Cancers: A Meta-Analysis and Systematic Review

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**Purpose:** Nodal staging of a patient with esophageal cancer predicts prognosis and directs therapy. The published data on accuracy of endoscopic ultrasound (EUS) for diagnosing nodal invasion in patients with esophageal cancer has been inconsistent.

**Aim:** To evaluate the accuracy of EUS in diagnosing mediastinal nodal metastasis of esophageal cancers.

**Methods: Study Selection Criteria:** Only EUS studies confirmed by surgery or prolonged followup were selected.

**Data collection & extraction:** Articles were searched in Medline, Pubmed, and Cochrane controlled trials registry. Two reviewers independently searched and extracted data.

**Statistical Method:** Meta-analysis for the accuracy of EUS was analyzed by calculating pooled estimates of sensitivity, specificity, likelihood ratios, and diagnostic odds ratios. Pooling was conducted by both fixed and random effects models. The heterogeneity of studies was tested using Cochran's *Q* test based upon inverse variance weights. Publication bias was estimated by Harbord-Egger and Begg-Mazumdar bias indicator.

**Results:** Initial search identified 2610 articles, in which, 360 relevant articles were selected and reviewed. Data was extracted from 44 studies (*N* = 4398) that met the inclusion criteria. Pooled sensitivity of EUS in diagnosing nodal involvement by esophageal cancers was 84.7% (95% CI: 82.9–86.4). EUS had a pooled specificity of 84.6% (95% CI: 83.2–85.9). The positive likelihood ratio of EUS was 3.34 (95% CI: 2.62–4.25) and negative likelihood ratio was 0.24 (95% CI: 0.91–0.30). The diagnostic odds ratio, the odds of having nodal metastasis in positive as compared to negative EUS studies, was 19.05 (95% CI: 12.72–28.52). All the pooled estimates, calculated by fixed and random effect models, were similar. SROC curves showed an area under the curve of 0.91. The *P* for chi-squared heterogeneity for all the pooled accuracy estimates was > 0.10. Harbord-Egger bias indicator was 1.08 (95% CI: -0.79–2.95, *P* = 0.29). The Begg-Mazumdar indicator for bias gave a Kendall's tau b value of 0.13 (*P* = 0.36).

**Conclusion:** EUS is an important and accurate diagnostic tool to evaluate nodal metastasis of esophageal cancers. This meta-analysis shows that EUS has a high specificity and sensitivity. EUS is an excellent diagnostic test to diagnose nodal metastasis of esophageal cancers.

## 1126

### Upper GI Cancer Assessment "Straight-to-Test" Service: A Safe, Efficient, and Cost-Effective Approach

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**Purpose:** Rapid access to diagnostics is key to early diagnosis of upper gastro-intestinal (UGI) cancer. Due to rising healthcare costs, there is also increasing pressure on gastroenterologists to cut the costs of treatment. In the UK, Cancer Plan 2000 requires all suspected cancer patients to be seen by specialists within 2 weeks of referral, and diagnostics must be completed within 31 days. These targets put huge service delivery challenges for most hospitals with limited resources. We started a "straight-to-test" (STT) service to reduce time to diagnosis and staging of suspected UGI cancer. On receiving referrals, patients were booked directly for upper endoscopy or ultrasound as appropriate. Clinic appointment was booked after the test, if necessary. There were no extra costs for setting.

**Methods:** A prospective study of new STT service over 12 months to study safety, efficiency and cost-effectiveness. All consecutive patients referred by GPs for UGI cancer assessment were studied. The patients were followed up for 6 months after endoscopy by telephonic interview and/or review of hospital medical records. Data included demographics, symptoms, endoscopy findings, follow-up plans and clinical outcomes at 6 months. The cost savings were calculated using Outpatient Mandatory Tariff Coding System.

**Results:** 241 patients (116 m, 125 f) were referred, of which 95% had endoscopy and/or imaging within 2 weeks. The commonest symptom was dyspepsia (68%), followed by dysphagia (48%), and anorexia (41%). The endoscopy diagnoses were Gastritis (32%), Hiatus hernia (26.9%), Oesophagitis (16.8%), duodenitis (12%), Cancer 27 (11.2%) and Gastric ulcers (2.4%). Cancers included oesophageal 15, gastric 4, pancreas 3, liver 2, and colon 3. 107 (44.3%) were discharged back to GP and 134 (55.7%) were followed up. Excluding cancer patients there was no significant difference between the 2 groups in clinical outcomes. There were no missed cancers. 31-day targets were achieved in all cancer patients. STT service saved 107 new (@£188 each) and reduced 134 follow-up (@£93 each). The net saving was £31373 over 12 months.

**Conclusion:** Our study shows that STT service for UGI cancer assessment is safe, efficient and highly cost-effective. The study also showed that more patients could be discharged back to GPs after cancer is excluded on gastroscopy and hence there is scope for more cost savings. STT model of cancer assessment service has potential for widespread use in NHS and other healthcare systems.

## 1127

### Accuracy and Clinical Impact of EUS – FNA as the Definitive Diagnostic or Staging Study in Patients with Suspected or Known Lung Cancer

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**Purpose:** Prognosis and management of non-small cell lung cancers (NSCLC) are dependent on accurate staging for metastatic lymphadenopathy (LAD). Endoscopic ultrasound guided fine needle aspiration (EUS-FNA) of mediastinal nodes has emerged as a valuable minimally invasive alternative for staging.

The objective of this study was to retrospectively determine the accuracy of EUS-FNA of mediastinal LNs in patients with known or suspected NSCLC and of mediastinal LAD of unknown etiology and review its clinical impact. Also, determine the diagnostic yield of using EUS-FNA as a primary modality for diagnosis and staging in patients with mediastinal LAD with lung mass on imaging.

**Methods:** A retrospective chart review was performed on all 107 patients that were identified. The EUS-FNA diagnosis was accepted as malignant mediastinal LNs when cytology was positive by EUS. When cytology was

non-malignant, the results were compared with the final surgical pathology of the excised LNs.

**Results:** There were 79 patients who had mediastinal LAD with known or suspected lung cancer by CT and 69 patients underwent FNA of suspicious nodes. 32 of 69 patients (46%) received a diagnosis of metastatic disease with EUS-FNA and did not undergo further invasive workup. 37 patients had benign or non-diagnostic FNAs of which 26 patients underwent surgical staging. Sensitivity, specificity and accuracy for EUS-FNA of mediastinal LAD in patients with known or suspected lung cancer was 84%, 100% and 90% respectively. The negative predictive value was 79%, the false negative rate was 15% and the positive predictive value was 100%.

There were 20 patients with suspicious mediastinal LAD of uncertain etiology. The diagnostic yield of EGD/EUS-FNA in patients with mediastinal LAD of unknown etiology was 95% (19 of 20 patients). 27 patients had mediastinal LAD with lung mass on CT scan without a tissue diagnosis of the primary tumor. Diagnosis and staging was made in 15 patients (56%) thus avoiding further invasive workup.

**Conclusion:** EUS-FNA of mediastinal LNs has a high accuracy with a high NPV and low false negative rate. Our data supports the use of EUS-FNA early in the work-up of mediastinal LNs thus avoiding unnecessary imaging, more invasive mediastinal sampling procedures and potentially futile surgery.

## 1128

### Risk Factors for Hypoxemia during Elective Outpatient Endoscopy

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**Purpose:** Cardiopulmonary events account for 50% of all adverse events during routine gastrointestinal endoscopy. Hypoxemia is the most common precursor of such events. There is paucity of data about the risk factors of hypoxemia during endoscopy. Thus, we conducted a post-hoc analysis from a prospective observational study of procedural sedation to assess the risk factors of hypoxemia.

**Methods:** The study enrolled patients with ASA class I-II for monitoring sedation during outpatient endoscopy. All patients received sedation by a combination of a narcotic and benzodiazepine. None of the patients received oxygen at the start of the procedure. Hypoxemia was defined as oxygen saturation  $\leq 90\%$  anytime during the procedure. Pre-procedure evaluation included demographics while intra-procedural evaluation included timing and dosages of medications and occurrence of hypoxemia. Univariable and multivariable analyses were performed for predetermined clinical variables and interactions were assessed among all the significant variables. The relationship of the velocity of meperidine and midazolam (mg/min) administration to the development of hypoxemia was explored.

**Results:** A balanced procedural cohort of 80 patients (20 each for EGD, colonoscopy, EUS, ERCP) were included in the study. The median age was 62 years (interquartile range IQR 50–74) while the median body mass index (BMI) was 25.7 (22.9–29.1). The proportion of obese (BMI  $\geq 30$ ) and non-obese (BMI  $< 30$ ) patients with hypoxemia were 71% (10/14) and 46% (30/65), respectively ( $P = 0.08$ ). On univariable analyses, significant risk factors for hypoxemia were BMI ( $P = 0.04$ ) and age  $\geq 60$  years ( $P = 0.03$ ). On multivariable analysis, the odds ratios (95% confidence intervals) for the development of hypoxemia were: age  $\geq 60$  years 4.5(1.4–14.3)  $P = 0.01$ ; BMI [1 unit increment] 1.1(0.99–1.2), [study range] 10.8(0.98–151)  $P = 0.07$ ; and meperidine dose (25 mg) 2.6(1.02–6.6)  $P = 0.04$ . There were no significant interactions among these variables. Even though hypoxemia was more common in procedures with longer duration, the velocity of meperidine and midazolam administration did not differ significantly between the patients with or without hypoxemia.

**Conclusion:** Age  $\geq 60$  years, BMI and meperidine dose appear to be significant risk factors for hypoxemia during routine outpatient endoscopy although BMI lost its significance marginally in multivariable analysis possibly due

to study sample size. A larger study is needed for the further exploration of these variables as predictors of hypoxemia.

## 1129

### A Single-Center Experience with 652 Cases of Wireless Capsule Endoscopy over a Period of 5 Years

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**Purpose:** Wireless Capsule Endoscopy (WCE), a relatively new diagnostic modality provides direct visualization of the entire small bowel mucosa. Its impact on patient care and usefulness in clinical practice has steadily been gaining ground. WCE is superior to barium radiography, push enteroscopy and CT scan of abdomen for the detection of small bowel diseases (Triester et al. A meta-analysis of the yield of WCE compared to other diagnostic modalities in patients with OGIB. Am J Gastroenterol. 2005;100:2407–18).

**Aim:** To assess: 1) The data on the frequency of various indications and small bowel mucosal abnormalities observed by WCE. 2) The diagnostic yield of WCE for various indications.

**Methods:** In this retrospective study, data is collected from 652 cases of WCE performed during the last 5-year period (2002–2007). Patients presented with various indications underwent WCE according to standard protocols.

**Results:** Total cases: 652 (Males = 311, Females = 341) A) Most common indication = Iron deficiency anemia (65%) B) Most common finding = Small bowel erosion (29%) C) Diagnostic yield of WCE for: 1) Iron deficiency anemia = 58% (244/424 cases) 2) OGIB = 62% (177/286 cases) D) Active bleeding in small bowel = 10% (63/652 cases) which was successfully thermo-coagulated by push enteroscopy.

**Conclusion:** 1) WCE played a major role in the detection of small bowel mucosal diseases in patients presented with various indications. 2) With a high diagnostic yield, WCE is the procedure of choice in patients with iron deficiency anemia and OGIB. 3) In a small number of patients (10%) where active bleeding was seen in small bowel, WCE resulted in the immediate change of management.

#### Indications of WCE (Total cases = 652)

Indications	No. of patients
Iron deficiency anemia	424 (65%)
OGIB	286 (44%)
Unexplained abdominal pain	100 (15%)
Suspected Crohn's disease	68 (10%)
Chronic diarrhea	61 (9%)
Suspected Celiac disease	5 (0.8%)
Polyposis syndrome	5 (0.8%)

Multiple indications are present in few cases

#### Small bowel findings observed by WCE (Total cases = 652)

Findings	No. of patients
Erosion (<5 mm in diameter)	192 (29%)
Ulceration (> 5 mm in diameter)	147 (23%)
Lymphangiectasia	144 (22%)
Angiodysplasia (AVM)	111 (17%)
Normal	91 (14%)
Active bleeding	63 (10%)
Polyp	50 (8%)
Nodular Lymphoid Hyperplasia	30 (5%)
Celiac disease	19 (3%)
Sub-mucosal bulge	22 (3%)
Tumor	7 (1%)

Multiple findings are present in few cases

1130

### Problems, Complications and Failures of Wireless Capsule Endoscopy: A Single-Center Experience with 652 Cases

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**Purpose:** Wireless Capsule Endoscopy (WCE), a relatively new diagnostic modality has provided direct visualization of the entire small bowel mucosa. Approximately over 400,000 patients worldwide have undergone WCE since its availability in 2001 (Given Imaging data, 2007). The problems related to WCE can be divided into technical limitations and failures secondary to malfunctioning of equipment and patient related complications and failures. A previous study from Europe based on data from 4 large referral centers has been reported on complications and limitations of WCE (Rondonotti et al. Gastrointest Endosc 2005;62:712–6).

**Aim:** The aim of this study is to identify the frequency and nature of complications, limitations and failures of WCE.

**Methods:** In this retrospective study, data is collected from 652 consecutive patients who underwent WCE during the last 5-year period (2002–2007). Patients presented with various indications underwent WCE according to standard protocols.

**Results:** Total cases: 652 (Males = 311, Females = 341) Total complications/failures = 96 out of 652 (15%) cases.

Most common complication = Incomplete small bowel examination (11%).

**Conclusion:** WCE in this large single center series has shown excellent utility with a limited number of technical failures and complications. [figure1]



Technical failures of WCE

Type of failure	No. of patients (Total cases = 652)
Battery failure	22 (3%)
Download failure	2 (0.3%)

Clinical limitations and complications of WCE

Types of limitation	No. of patients (Total cases = 652)
Inability to swallow the capsule	3 (0.5%)
Incomplete small bowel examination secondary to:	69 (11%)
A) Capsule stayed in Esophagus	5 (0.8%)
B) Delayed gastric emptying	31 (5%)
C) Retained food particles/bile in small bowel obscuring the images	30 (5%)
D) Retained capsule secondary to:	3 (0.5%)
1) Stricture secondary to Crohn's disease	1
2) Intussusception secondary to Celiac disease	1
3) Small bowel tumor	1
Total Complications/failures	96 (15%)

1131

### Novel Endoscopic Techniques for Stoma Size Reduction Following Gastrojejunostomy

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**Purpose:** Although significant weight loss can follow gastric bypass surgery, over time some patients reach a plateau or begin to regain weight. One explanation has been that the gastro-jejunal anastomosis may have enlarged and reduction of stoma size might permit additional weight loss. The technique of directed hollow-needle t-tag suturing has been described for endoscopic procedures including oversew of ulcers, closure of luminal defects, and creation of enteric anastomosis. We describe the use of this technique for simple sutured or patch closure of gastrojejunostomies in an animal model.

**Methods:** 6 common farm pigs (30–35 kilos) underwent laparotomy and creation of a gastrojejunostomy. Following recovery (8 to 14 days) the pigs underwent upper endoscopy and the stoma size was measured using a calibrated rotatable catheter. (1) *Suture closure:* Bicap cautery was applied to the gastric mucosa surrounding the anastomosis, and this area was brushed to remove mucosa. Using a hollow-needle and backloaded t-tag suturing system passed through the endoscope, multiple sets of stitches were placed to effect closure of the gastro-enteric stoma. These were located within 1 cm of the stoma edges and about 5 mm apart. The anastomosis was measured at the conclusion of the procedure. (2) *Patch Closure:* In 3 pigs, an impermeable patch with a central hole of 5 mm diameter was sutured to the edges of the GJ stoma using the t-tag system.

**Results:** Open surgical gastro-jejunostomies were successfully created in 6 pigs. Baseline anastomotic diameters ranged from 28 to 32 mm. *Sewing:* Closure of the stoma was successfully accomplished in all cases, requiring 4 sets of stitches. Suture approximation was accomplished with a cinching/cutting catheter placed through the endoscope channel. Final anastomotic size was reduced to 4–5 mm. *Patch:* 3 pigs were treated with patches fixed with 6 to 8 pairs of threads and locks.

**Conclusion:** Large gastro-jejunostomy anastomotic openings can be easily, safely, accurately and effectively reduced in size using directed t-tag sewing methods for simple sutured or patch closure. The precision in placing stitches with this new technique offers an advantage over other endoscopic sewing methods. This endoscopic sewing method may be useful for bariatric patients with dilated gastro-enterostomies and further clinical study is warranted.

1132

### Does Pre-Procedural Counseling by Peers Improve Completion Rates?

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**Purpose:** The aim of this study is to examine the relationship between improved health literacy and patient compliance with gastrointestinal procedures when pre-procedural counseling is provided by peers.

**Methods:** At an ambulatory clinic, the completion rate of 267 consecutive patients scheduled for 297 gastrointestinal procedures (colonoscopy, EGD, ERCP, EUS, or flexible sigmoidoscopy) who received pre-procedural counseling was compared with the completion rate of 326 consecutive patients scheduled for 331 procedures who did not receive this intensive counseling. A second comparison was made between groups that compared adherence to the originally scheduled appointment among those patients who followed up for their procedure.

**Results:** Pre-procedural counseling increases the completion rate of EGD (85.9% compared to 74.6) but does not increase overall colonoscopy

completion rates (70.3% compared to 70.8%). However, patients who have received pre-procedural counseling are more likely than those who have not received counseling to attend their originally scheduled appointment, regardless of the type of procedure (75.3% compared to 56.2% for EGD; 64.6% compared to 56.2% for colonoscopy).

**Conclusion:** Providing patients who may have limited health literacy with pre-procedural counseling can help improve timely completion of necessary gastrointestinal procedures. Counseling significantly improves patient compliance with EGD and compliance with originally scheduled EGD and colonoscopy appointments, while overall compliance with colonoscopy remains poor.

### 1133

#### Diagnostic Yield of Wireless Capsule Endoscopy for the Evaluation of Iron Deficiency Anemia in Different Age Groups

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**Purpose:** Obscure gastrointestinal bleeding (OGIB) could be the source of iron deficiency anemia in patients with normal EGD and colonoscopy. WCE helps in the detection of small bowel mucosal abnormalities such as erosions, ulcerations, angiodysplasia and celiac disease resulting in OGIB and iron deficiency anemia.

**Aim:** The aim of this study is to identify the source of bleeding (OGIB) in the small bowel resulting in iron deficiency anemia with the help of WCE and also to evaluate its diagnostic yield in different age groups.

**Methods:** In this retrospective study, data is collected from 652 consecutive patients who underwent WCE during the last 5-years (2002–2007). Iron deficiency anemia is defined on the basis of low serum ferritin levels (<15 mg/L) and low transferrin saturation (<20%).

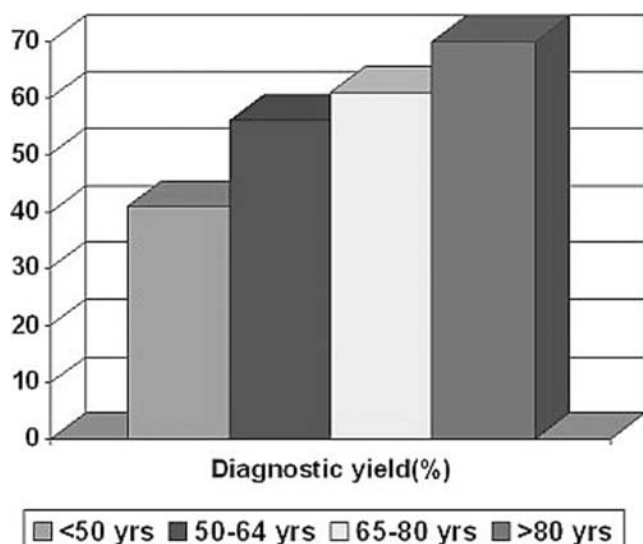
**Results:** Total cases: 652 (Males = 311, Females = 341).

Diagnostic yield of WCE for iron deficiency anemia in different age groups:

- 1) < 50 yrs = 41%
- 2) 50–64 yrs = 56%
- 3) 65–85 yrs = 61%
- 4) > 85 yrs = 70%

#### Conclusion:

1) Iron deficiency anemia is a frequent indication for WCE especially in the older adults (age > 65).



2) The diagnostic yield of WCE in the evaluation of OGIB resulting in iron deficiency anemia progressively increases as age advances.

3) Small bowel erosions, ulcerations and angiodysplasia are the most frequent findings in patients with iron deficiency anemia.

4) Active bleeding in the small bowel was seen mostly in older adults, resulting in an immediate change of management and outcome.[figure1]

Diagnostic yield of WCE for evaluation of iron deficiency anemia in all age groups

Age	< 50 yrs	50–64 yrs	65–85 yrs	> 85 yrs
No. of patients	169 (26%)	166 (25%)	281 (43%)	36 (6%)
Patients with iron deficiency anemia	58 (34%)	122 (74%)	217 (77%)	27 (75%)
SB Erosion (< 5 mm in diameter)	10 (17%)	37 (30%)	73 (34%)	10 (37%)
SB ulceration (> 5 mm in diameter)	11 (19%)	27 (22%)	44 (20%)	7 (26%)
Angiodysplasia (AVM)	3 (5%)	16 (13%)	44 (20%)	10 (37%)
Active bleeding in SB	4 (7%)	12 (10%)	30 (14%)	2 (7%)
Celiac disease	8 (14%)	4 (3%)	6 (3%)	1 (4%)
Diagnostic yield	41%	56%	61%	70%

### 1134

#### Retrospective Comparison of In-Hospital Rebleeding Rates in Non-Variceal UGI Bleeding Demonstrates the Superiority of Clips Therapy over Injection and/or Thermocoagulation

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**Purpose:** Endoscopic intervention is recommended in patients with non-variceal acute UGI bleeding (NVAUGIB) when active bleeding or stigmata of higher risk of rebleeding are noted at the time of initial endoscopy. Opinions regarding the best method of achieving hemostasis and reducing the risk of rebleeding differ. We retrospectively studied the charts of such patients who were admitted to our institution from 2005 to 2006 to determine which of the modalities in NVAUGIB achieved lower rebleeding rates. In particular, we wanted to compare the use of endoscopic clips with or without injection therapy to the use of thermocoagulation and/or injection therapy.

**Methods:** Patients were included in the study only if active bleeding, oozing, visible vessel, or sentinel clot was seen on initial EGD and therapeutic intervention occurred. The patients were divided into two groups. Patients with use of endoscopic clip with or without injection therapy were placed in Group A and patients with thermocoagulation and/or injection therapy (but not endoscopic clips) were placed in Group B. Only the in-hospital rebleeding rate was assessed. Rebleeding was documented either by convincing clinical picture or by endoscopic evidence.

**Results:** A total of 213 patients met the inclusion criteria. 78 patients were placed in Group A. None of the patients in Group A had rebleeding (0/78). 135 patients fell into Group B. Eight patients in Group B (8/135, 5.9%) rebled, with one requiring surgery. This agrees with previously published data. The rebleeding rate of 0% in Group A was significantly lower than in Group B ( $P$  value <0.03 using one-sided Fisher's exact test). Both groups A and B had comparable proportions of patients with visible vessel or active bleeding (44.87% for Group A compared to 45.19% for Group B).

**Conclusion:** In non-variceal acute UGI bleeding, the use of endoscopic clips alone or in combination with injection therapy is associated with a lower in-hospital rebleeding rate than is thermocoagulation and/or injection therapy without endoscopic clip therapy. Endoscopic clips should be regarded as the therapy of choice in NVAUGIB. Injection therapy alone or combination therapy with injection and thermocoagulation for NVAUGIB should be reserved for those situations where the application of endoscopic clips is not feasible or not successful and when the clips are not available.

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### EUS Findings of a Pancreatic Schwannoma Presenting as a Cystic Lesion: A Case Report

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**Purpose:** Pancreatic Schwannomas are extremely rare tumors. We here by describe a pancreatic Schwannoma that presented as a cystic mass and had unusual endosonographic features.

**History:** A 35 year old male presented with a 3 month history of epigastric pain radiating to back. CT scan of the abdomen revealed a 6 cm × 6 cm septated cystic lesion in the pancreatic body suggestive of a complex pseudocyst or less likely a cystic neoplasm. The patient underwent a linear EUS demonstrating a 7 cm complex multiloculated cystic mass with thick septations and a solid component. The patient was not considered to have a typical pseudocyst based on EUS findings and a cystic tumor of the pancreas was considered as the more likely diagnosis. Fine Needle Aspiration (FNA) of the cyst was not done to avoid the risk of seeding in case the mass was a malignant neoplasm as the patient was symptomatic and surgical resection was considered appropriate regardless of the EUS FNA findings. Surgery revealed a large, multiloculated mass with cystic and solid components and histopathology revealed it to be a Schwannoma with cystic degeneration and immunostaining for S100 was strongly positive, confirming the diagnosis. The patient recovered uneventfully and is symptom free six months after surgery.

Schwannomas arise from neural crest cells and are also known as neurilemmomas. Pancreatic Schwannomas are very rare and the reported cases have been around 40. More than half of them can undergo cystic degeneration and mimic pancreatic pseudo cysts or cystic neoplasms. 83% of Schwannomas are benign. EUS FNA is being increasingly used to diagnose pancreatic cystic lesions. It is not clear if there are any distinctive EUS findings in pancreatic Schwannoma. Schwannomas should be considered in the differential diagnosis of pancreatic cystic lesions or cystic lesions in patients with Neurofibromatosis. [figure 1]



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### Visualizing the Ampulla of Vater Using a Forward Viewing Endoscope

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**Purpose:** The frequency of seeing the ampulla using a forward-viewing endoscope is unknown. Many gastroenterologists note seeing the ampulla on an inconsistent basis during routine upper endoscopy. Here, we attempt to determine the frequency of ampullary visualization during routine upper GI endoscopy with a forward-viewing endoscope.

**Methods:** February through April 2007, 224 patients underwent upper endoscopy using a forward viewing endoscope (Olympus GIFH180) for various indications: anemia, GERD, dysphagia, malabsorption, neoplasia (Polypoid syndromes, Barrett esophagus), etc. The endoscope was advanced to 3rd portion of the duodenum, and if the ampulla was visualized, photo documentation was obtained. Similarly, if the ampulla was not visualized, it was reported as such. The upper endoscopies were performed by five gastroenterologists whom have advanced training/experience with upper endoscopy and ERCP.

**Results:** A total of 224 patients underwent esophagogastroduodenoscopy. Of the 224 patients, seven patients have a history either of Whipple Procedure, Billroth II or Gastric Bypass surgery. These patients were excluded from final analysis of the data. The ampulla of Vater was identified in 154(70.9%) of 217 patients, while in remaining 63(29%) of 217 patients, the ampulla was not identified. When the ampulla was identified, the average insertion depth of the instrument was 62.9 cm. In addition, three patients were found to have benign villous adenoma at the ampulla. For the 224 esophagogastroduodenoscopies that were completed in these patients, there were no complications or prolongation of procedure time.

**Conclusion:** The ampulla of Vater can be visualized in the majority of patients undergoing routine upper GI endoscopy on an outpatient basis. While Kong et al, were able to detect the duodenal papilla via capsule endoscopy in 43.6% of 112 cases in their retrospective review, we were able to identify and document seeing the ampulla of Vater 70.9% of the time using a forward viewing endoscope. In this study, three ampullary adenomas were coincidentally detected. A larger study is needed to determine if there is a difference in ampullary identification based on the level of gastroenterologist training and years of experience. Furthermore, if gastroenterologists start to routinely identify the ampulla and biopsy as needed, the risks and benefits related to the detection of ampullary neoplasms will have to be assessed.

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### A Retrospective Study of Capsule Endoscopy at a Tertiary Care Center: Inpatient Versus Outpatient Populations

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**Purpose:** We intended to analyze the results of small bowel capsule studies performed at one tertiary medical center. The primary aim was to evaluate the inpatient and outpatient populations for completeness of study and adequate small bowel visualization. The effect of diabetes on capsule studies was also evaluated.

**Methods:** A chart review of 108 consecutive patients undergoing capsule endoscopy from September 2003-September 2005 was carried out using the electronic medical record. Statistical analysis was determined using chi-square method.

**Results:** The most common indication for CE was obscure gastrointestinal bleeding. The most common small bowel finding was AVMs. Capsule retention rate was 8.3%. Suboptimal visualization of the small intestine due to poor bowel preparation was found in 15.7% of studies. The frequency of suboptimal studies was not different between inpatient and outpatient cases ( $P = 0.62$ ). Seventy-seven studies (71.3%) were completed with capsule entering the cecum. Accurate location of 5 studies (4.6%) could not be determined at the end of the study. The proportion of incomplete inpatient studies was not different from the outpatient population ( $P = 0.76$ ). The presence of diabetes did not effect study completion ( $P = 0.87$ ).

**Conclusion:** A difference between the inpatient and outpatient populations with regard to completion of a study or ability to visualize small bowel mucosa was not found. Proposal for use of prokinetic agents and bowel preparation could not be supported for the inpatient population. In addition, diabetes did not appear to be a risk factor for completeness of a study. Therefore, using prokinetic agents or placement of the capsule beyond the pylorus with a gastroscope could not be justified.

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### High-Definition White Light and High-Contrast Narrow-Band Imaging at Standard Magnification To Predict Polyp Histology: An In-Vivo Study

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**Purpose:** High-contrast imaging (HCI) can predict polyp histology using high-magnification endoscopes. A prospective, in-vivo study was performed to determine if high-definition white light (WL) and narrow-band HCI without magnification can predict polyp histology during colonoscopy.

**Methods:** Subjects without risk factors for neoplastic polyps undergoing routine screening colonoscopy were eligible. Four endoscopists performed the procedures with Olympus CF-H180 AL/I colonoscopes and activated narrow band imaging (NBI) with an endoscopic button. Polyp size (<10 mm were included) and location were first recorded. Using WL, the presence or absence of cerebriform pit pattern or prominent vascular markings (typical of neoplastic polyps) were noted and histology predicted: neoplastic or non-neoplastic. Confidence in the histological assignment and image quality were rated on a 5-point Likert scale. The process was repeated using HCI.

**Results:** 55 subjects (58% female, mean age 58.6 years, range 45–85) with 93 polyps (56 neoplastic/37 non-neoplastic) were enrolled. The mean polyp size was 4.7 mm  $\pm$  1.8, (range 2–10). The sensitivity, specificity, PPV, NPV and accuracy of WL was 68%, 84%, 87%, 63% and 74% compared to 85%, 81%, 87%, 79%, and 84% for HCI. HCI improved the endoscopists' ability to determine histology in 9/56 (16%) neoplastic polyps. In 4 non-neoplastic polyps, HCI incorrectly changed histology to neoplastic. In no cases was a correct WL neoplastic designation changed to a non-neoplastic designation by HCI. The mean histological confidence scores were 3.3  $\pm$  1.1 for WL and 4.1  $\pm$  0.8 for NBI ( $P < 0.0001$ ). The mean image quality scores were 3.9  $\pm$  1.3 for WL and 4.4  $\pm$  0.7 for HCI ( $P < 0.0001$ ). Among correctly assigned neoplastic polyps, HCI visualized prominent vascular or cerebriform patterns in 85% of polyps compared to 0% among incorrectly assigned neoplastic polyps. Neither polyp size nor location influenced histological designations.

**Conclusion:** To our knowledge, this is the first real-time evaluation of HCI at standard magnification in determining polyp histology. HCI is a facile technology that was 16% more sensitive in identifying neoplastic polyps compared to WL. HCI also allowed for significantly more confidence in the initial assessment of histology as well as better image quality. Although useful, HCI without magnification is not accurate enough to replace histology.

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### Does Scheduling Time Matter? 30 Minute Versus 60 Minute Intervals for Colonoscopy

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**Purpose:** Colonoscopy is the gold standard screening tool for the detection of colonic neoplasia. To accommodate the increasing demand of colonoscopy many endoscopy centers have increased the number of procedures performed

per day by decreasing the allotted time intervals. In April of 2004, our institution allowed one-hour time intervals to be decreased to 30 minute intervals. The objective of our study is to determine if adenoma detection rate is decreased by the change in allotted procedure time.

**Methods:** We performed a retrospective chart review of all screening colonoscopies performed in 2003 (60 minute intervals) and 2005 (30 minute intervals) to compare the adenoma detection rate. Patients were excluded if there was family or personal history of colon polyps or colon cancer, personal history of inflammatory bowel disease, or if the patient had rectal bleeding. Physicians who had more than 100 screening colonoscopies during 2003 and 2005 were included in the study. Age, sex, endoscopist, total number and size of polyps found was recorded. Pathology reports were reviewed for all procedures where polyps were found. Histologic type of polyp was recorded from the pathology reports.

**Results:** 22 physicians performed screening colonoscopies in 2003 and 2005. Only 8 physicians were identified as having more than 100 procedures during each year of the study period. These 8 physicians performed a total of 1531 screening colonoscopies in 2003 and 1610 screening colonoscopies in 2005. The mean patient age was 60.18  $\pm$  8.86 in 2003 and 59.58  $\pm$  8.8 in 2005 ( $P = 0.059$ ). The % of patients that were male were 47.3 in 2003 and 46.7 in 2005 ( $P = 0.744$ ). The % of colonoscopies where at least one adenoma was found, mean number of adenomas per colonoscopy, mean number of hyperplastic polyps per colonoscopy, and mean number of advanced adenomas per colonoscopy for these 8 physicians is reported below.

**Conclusion:** Reducing the scheduling interval for endoscopic procedures from 60 minutes to 30 minutes does not affect adenoma detection rates.

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### Capsule Endoscopy Performed for Small Bowel Obstruction: A Tertiary-Referral Center Experience

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**Purpose:** It is suggested that the use of capsule endoscopy (CE) in patients with known or suspected small bowel obstruction is contraindicated. We describe the experience of a tertiary referral center's use of CE for the specific indication of small bowel obstruction.

**Methods:** From November 2003 to May 2007 at the University of North Carolina Hospitals, 54 CE studies were performed for the evaluation of small bowel obstruction in patients whom were being evaluated for operative intervention. We retrospectively reviewed the medical records and CE findings of these patients.

**Results:** The majority of the population was female (57%) and Caucasian (77.8%). The median age (Q1, Q3) was 48.9 years (38.7, 62.0). Most (87%) of the studies were done on an outpatient basis. Approximately 1/3 of patients had inflammatory bowel disease, 68% of which had Crohn's disease. Recent (within 7 days) or ongoing obstruction was the indication for CE in 24% of patients; the remainder done for chronic or recurrent obstruction. The median (Q1, Q3) duration of obstructive symptoms prior to CE was 210 days

Pooled polyp detection rates 8 busiest endoscopists\*

	2003	2005	P value
% procedures with adenoma detection	22.91 $\pm$ 8.2	23.39 $\pm$ 7.2	0.678
# adenomas per procedure	0.37 $\pm$ 0.18	0.33 $\pm$ 0.15	0.113
# hyperplastic polyps per colonoscopy	0.26 $\pm$ 0.15	0.26 $\pm$ 0.10	0.934
# of advanced adenomas per colonoscopy	0.037 $\pm$ 0.013	0.041 $\pm$ 0.014	0.517

\* Plus-minus values are means  $\pm$  SD

(60, 1460). Most (75.9%) patients had a history of prior abdominal surgery, 20% had been previously treated with pelvic external beam radiation, and 20% had NSAID use documented at the time of CE. Radiography revealed obstruction in 32 patients (59%) prior to CE, with 24 patients (44%) having obstruction on abdominal CT or small bowel barium study.

CE diagnosed potential obstructing lesions in 29 patients (54%), and 25 patients (46%) underwent surgery a median (Q1, Q3) of 20 days following CE (10.5, 55.5). Surgery after CE was diagnostic of an obstructing lesion in 95% of these patients. The capsule reached the cecum in 35% of patients. CE retention occurred in 10 patients (18.5%), with CE removal at surgery in 8 of these (14.8%). There were no perforations, emergent surgeries, or other complications after CE. CE findings agreed with operative assessment of the culprit obstructing lesion in 17 of the 25 patients whom underwent surgery (68%). No preoperative, clinical factors were significantly associated with odds of agreement between CE and surgical findings.

**Conclusion:** CE is safe and effective in selected patients with known or suspected small bowel obstruction, based upon this review of a single tertiary center's experience.

## 1141

### Disappointing Yield of Duodenal Biopsies for Celiac Disease in "At Risk" Patients

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**Purpose:** Celiac Disease is a relatively common disease in people of European ancestry with a prevalence of around 0.5–1%. The prevalence of CD in United States is estimated to be around 1 in 133 people. CD is thought to be an under diagnosed disease with a ratio of 7:1 (undiagnosed:diagnosed). Screening serological tests are available but duodenal biopsies are considered to be the gold standard. Iron Deficiency Anemia (IDA), diarrhea, dyspepsia, malabsorption are some of the common GI manifestations of CD. Many authors recommend routine duodenal biopsies in the above "at risk" patients. Most of the studies are from Europe where the prevalence of CD is higher than in the United States (USA).

**Aim:** To study the diagnostic yield of duodenal biopsies for CD in a teaching hospital in the US

**Methods:** Retrospective database review of all consecutive duodenal biopsies obtained to "rule out celiac disease" from June 2005 to June 2007. Indications, endoscopic features and pathology reports were reviewed

**Results:** A total of 338 duodenal biopsies for CD were performed during the two year time period in 138(41%) males and 200(59%) females. Ethnicity wise 57% were caucasians followed by 25% African Americans and 14% hispanics. Indications to suspect celiac disease were IDA in 51.75%(175/338), diarrhea in 22%(75/338), dyspepsia in 20/338(5.9%), weight loss in 18/338(5.3%). Reasons for suspecting CD were unknown in 10% patients. Among these patients only 4/338(1.1%) had serological testing prior to endoscopy and 2/338(0.5%) had positive serology

**Among the 338 biopsies only 2 (2/338 = 0.6%) revealed CD.** 334/338 biopsies were interpreted as normal and 1/338 was interpreted as mild villous atrophy and 1/338 was interpreted as infectious duodenitis. In the two patients diagnosed with CD one of them had anemia and positive celiac serology prior to endoscopy and the second patient had severe diarrhea.

**Limitations:** All the inherent limitations of a retrospective study.

**Conclusion:** Since CD is thought to be an under diagnosed disease duodenal biopsies are recommended in patients presenting with "high risk" symptoms like diarrhea, IDA or weight loss or dyspepsia. Most of the data is based on European population with high prevalence of CD. In our study the yield of duodenal biopsies in patients with high risk symptoms is only 0.5%. Prospective studies in USA to evaluate strategies like pre endoscopy serological screening are needed.

## 1142

### Efficacy of Digital High Contrast Imaging Coupled with Standard Colonoscopes in Predicting Colon Polyp Histology

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**Purpose:** Recent data has shown digital high-contrast imaging (HCI) technologies to be useful in predicting colon polyp histology when using high-magnification endoscopes. Little data exists on the ability of HCI to predict polyp histology with standard endoscopes. As non-magnifying endoscopes are widely available in standard practice settings, we performed a study to compare the accuracy of (narrow band) HCI and high definition white light (WL) images in predicting polyp histology without the use of high magnification endoscopes.

**Methods:** We used HCI endoscopes and processors (Olympus CV180 with Narrow Band Imaging™) to visualize colonic polyps in patients undergoing elective outpatient colonoscopy. Static digital images of polyps were collected in both HCI and WL and polyp size and location were recorded. Histology was later collected. Images were then assembled into power point slide shows stratified by imaging modality. These were reviewed by 2 endoscopists blinded to all patient and polyp information, on a standard 19 inch LCD monitor. Polyps were designated as either neoplastic or non-neoplastic, based on pit patterns and presence of vascular markings. Predictions were compared to histopathology as the gold standard. Image quality and reader confidence were graded on a 5-point Likert scale with a score of 5 being highest.

**Results:** Separate WL and HCI images of 80 (49 neoplastic, 31 non-neoplastic) polyps from 63 patients were obtained. Mean polyp size was  $5.13 \pm 2.12$  mm ( $5.35 \pm 2.16$  neoplastic;  $4.42 \pm 1.78$  non-neoplastic ( $P = 0.02$ )). Pooling data from the 2 readers, HCI correctly predicted neoplastic histology in 93 of 98 images (sensitivity 95%, PPV 94%) while WL did so in 58 of 98 images (sensitivity 59%, PPV 80%). HCI correctly predicted non-neoplastic histology in 56 of 62 images (specificity 90%, NPV 92%) while WL did so in 47 of 62 image (specificity 76%, NPV 54%). Mean confidence scores for HCI ( $3.97 \pm 0.95$ ) and WL ( $2.71 \pm 0.95$ ) were significantly different ( $P < 0.0001$ ). Mean image quality scores for HCI ( $3.79 \pm 0.97$ ) was also higher than WL ( $3.14 \pm 0.92$ ) ( $P < 0.0001$ ).

**Conclusion:** HCI with standard endoscopes was more accurate in predicting colon polyp histology compared to WL. Confidence and image quality was significantly higher in the HCI group. Based on our findings, HCI at low magnification may be useful in predicting colon polyp histology.

## 1143

### Does Tandem Colonoscopy Affect the Adenoma Detection Rate Described with Narrow Band Imaging?

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**Purpose:** Narrow band imaging (NBI) is a novel endoscopic optical technique that enhances tissue details by narrowing bandwidth of transmitted light using optical filters. We previously demonstrated that using high definition endoscopes, NBI with magnification allowed for a higher adenoma detection rate compared to white light.

**Aim:** To determine whether the tandem nature of colonoscopy alone in our prior study contributed to the improved detection rate seen with NBI.

**Methods:** Patients referred for average risk CRC screening from 09/2006 to 06/2007 were studied. Olympus H180 scope series were used. All procedures were performed by 2 experienced gastroenterologists and a third year fellow. Patients underwent tandem colonoscopy following cecal intubation. Initial evaluation utilized the NBI mode and was then followed by re-evaluation using white light, performed segmentally every 15 cm. Cecal and withdrawal times were recorded. Detection of polyps by either WL or NBI as well as



their histology, size and anatomical location were recorded and compared. Students t test and Fishers exact test were used for statistical purposes.

**Results:** A total of 146 patients were evaluated, 100 patients in the NBI/HDM group and 46 patients in the WL/tandem group. All were men with mean ages of 62.2 and 60.4 respectively ( $P = \text{NS}$ ). A total of 22/74 (29.7%) additional polyps were detected by WL/tandem compared with 31/214 (14%) in the NBI/HDM group ( $P = 0.005$ ). Of the polyps “gained”, 13/22 (59.1%) were confirmed tubular adenomas in the WL/tandem group versus 11/31 (35%) in the NBI/HDM group ( $P = \text{NS}$ ). The majority of TAs detected in the WL/tandem group were 1–3 mm in size (8/13, 62%) and 4–6 mm in size (4/13, 31%). 69% were located more proximally. The WL/tandem group was associated with shorter withdrawal times (15.8 min vs 18.9 min,  $P = 0.003$ ), longer cecal intubation times (6.9 min vs 4.9 min,  $P < 0.005$ ) with similar total times (22.7 min vs 23.8 min,  $P = \text{NS}$ ). These differences may be explained by the addition of a fellow in the initial part of the procedures, with the tandem portions completed by the same 2 experienced gastroenterologists.

**Conclusion:** 1) The WL/tandem group detected significantly more polyps than the NBI/HDM group. 2) Although the tubular adenoma detection rate was also higher in the WL/tandem group, the difference was not statistically different. 3) This suggests that the tandem nature of the procedure by itself, may be a significant contributing factor for the increased polyp detection rate (irrespective of using WL or NBI).

#### 1144

##### CES E-Score for Esophageal Capsule Endoscopy Image Quality Assessment

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**Purpose:** The aim of this study was to develop and then validate a standardized grading scale to assess esophageal capsule endoscopy (ECE) video image quality.

**Methods:** We devised the Capsule Endoscopy Services Esophageal score (CES E-score) as a standardized grading scale to assess the quality of esophageal images obtained during ECE examinations. The CES E-score is comprised of an aggregate of 5 different parameters including visualized anatomic landmarks, duration of esophageal imaging, image quality, illumination, and artifacts (see Table 1).

A total of 318 de-identified ECE cases (GERD screening, N = 312; esophageal varices surveillance, N = 6) were independently scored by 2 gastroenterologists in a randomized, blinded fashion. Each of the 5 parameters were scored 0, 1, 2 based on the pre-defined criteria. The CES E-score was calculated by the total sum of points, ranging from 0 (poorest quality) to 10 (highest quality). Concordance rates between the two GI's were assessed for each parameter as well as aggregate score.

**Results:** The concordance rate was  $\geq 95\%$  for all parameters, and  $> 98\%$  for total score between the two GI's. The mean CES E-score was  $8.5 \pm 1.1$ . The median score was 9. The two major factors causing low scores were artifacts and incomplete visualization of anatomical landmarks (bubbles/particulate matter obscuring the distal esophagus). All scores were within 1 point for all parameters for the two investigators.

**Conclusion:** The CES E-Score is a highly reproducible and valid scale to assess the quality of ECE studies, and to identify areas for technological

improvement. This standardized scoring system can be a useful tool for future ECE studies.

#### 1145

##### Endosonographic Diagnosis of Gastric Variceal Bleeding

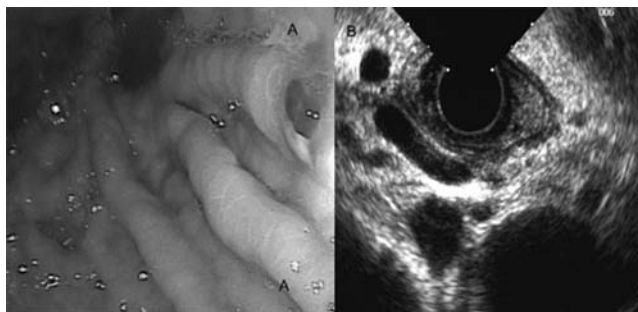
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**Purpose:** Gastric variceal bleeding remains a clinical challenge. Though the risk of bleeding from gastric varices is significantly less than esophageal varices, the transfusion requirements and mortality are significantly higher. Identification of gastric varices is of paramount importance as the management strategy is different from that of isolated esophageal varices.

Though identification of gastric varices is by endoscopic visualization, we describe a challenging scenario in which suspected gastric variceal bleeding was confirmed by endosonography.

Case: 56 y/o male with **alcoholic cirrhosis** was admitted for a recurrent episode of hematochezia, hypotension and anemia. Two previous upper and lower endoscopies for similar presentations had revealed esophagitis and no explanation for blood loss. Patient presented with 3 episodes of hematochezia 1 day earlier without syncope. Admission labs were significant for a Hb of 6 gm/dl (baseline 12), INR 1.4, Platelet count 46,000, T. Bili 2.7 gm/dl. Hemoglobin stabilized after admission with no further manifestations of GI bleeding. Following transfusion and initiation of octreotide infusions, EGD was performed which showed **grade 1 esophageal varices with no stigmata of recent bleeding** and no fresh or old blood in the stomach. Three **linear mucosal folds** traversed the lesser curvature from the GE junction. A small 5 mm ulcer with an adherent clot was located on one of the folds near the cardia. The remainder of the examination was normal. With suspicion of underlying varices *no endoscopic therapy was attempted to the ulcer*. The ulcer was examined with *mini probe ultrasonography* which showed a large submucosal gastric varix and numerous portosystemic collaterals near the GE junction. Radial EUS imaging further defined the *ulcer and the clot located directly overlying the vessel wall of a gastric varix*. The patient underwent urgent TIPS placement and has not had any recurrent bleeding.

**Conclusion:** Endosonography can play an important role in *identification of suspected gastric varices that are not obvious on direct endoscopic visualization*. [figure1]



CES E-Score Parameters	Score = 0	Score = +1	Score = +2
1. Anatomical Landmarks(a)	Non-visualized	Adequate	Good
2. Esophageal Transit Time(b) (seconds)	< 1	1–5	> 5
3. Image Quality (resolution/focus)	Poor	Adequate	Good
4. Illumination (Brightness/darkness)	Poor	Adequate	Good
5. Artifacts (bubble, food particle, and liquid)	All three	Any 1 or 2	None

(a) = Visualization of the distal esophagus and squamocolumnar junction (Z line) in its entirety (antegrade and/or retrograde views) (b) = Time from first esophageal image to first gastric image

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**Colonoscopy Procedure Times and Obesity: A Retrospective Review**

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**Purpose:** Obesity has now reached epidemic proportions in the United States. Its relationship to diabetes, hypertension, and various neoplastic processes are well documented, however its impact on endoscopic efficiency is not well studied. Obesity has been cited as a potential barrier to colon cancer screening, partly due to perceived procedural difficulty. Our goal is to determine obesity's effect on various endoscopic parameters.

**Methods:** Using the ProVation® MD nursing and physician databases we retrospectively reviewed data for all patients that underwent colonoscopy in our center from 2005–06. From the 4500 colonoscopies performed we excluded procedures with incomplete data, dual procedures, and procedures involving trainees, leaving 724 procedures performed completely by staff gastroenterologists. We calculated the exam time (defined as the time from scope insertion to complete withdrawal), cecal intubation time, procedure time (defined as start of sedation to complete withdrawal), and post procedure recovery time (defined as the time from complete withdrawal to discharge from center). The times were calculated for each patient, and the patients were divided into categories according to BMI as follows: <20, 20–24, 25–29, 30–34, >34. Significance was determined using analysis of variance.

**Results:** Obesity had no significant effect on exam time, cecal intubation time, procedure time, or recovery time. The mean procedural times are shown in the table.

**Conclusion:** Several studies demonstrate lower than average colon cancer screening in obese patients despite a higher rate of adenomas. Perceived technical difficulties and physician referral bias are possible causes for these lower rates. We have shown no increase in exam time, cecal intubation time, procedure time, and post procedure recovery time for the obese compared to those with BMI's ranging from 20–29. Perceived technical difficulties in performing screening colonoscopy in the obese are unfounded.

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**Role of Endoscopic Ultrasonography in the Evaluation of Gastric Submucosal Lesions: A Single Center Experience**

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**Purpose:** Gastric submucosal lesions are often seen on routine upper endoscopy. Endoscopic Ultrasound (EUS) is a valuable imaging modality for gastrointestinal submucosal lesions. It is helpful in accurately assessing layer of origin and can differentiate submucosal tumors from extragastric compression as well.

**Methods:** EUS procedures performed at our center from April 2002 to February 2006 were reviewed. Patients selected for this retrospective review underwent an upper abdominal EUS for further evaluation of gastric submucosal lesions or extragastric compression on endoscopy. Results were compared with CT scan and surgical pathology whenever possible.

**Results:** 47 patients underwent EUS for gastric submucosal lesions. EUS revealed stromal tumor arising from the muscularis propria in 42% (20/47).

The size varied from 8 mm to 7 cm. Two patients with tumor size more than 3 cm presented with upper gastrointestinal bleeding. EUS guided fine needle aspiration cytology revealed malignant stromal tumor in 3 patients, which was confirmed later on surgery. Other findings included pancreatic rest 3, lipoma 3, Dieulafoy 1, submucosal cyst 1, carcinoid 1 and non-specific cellular aggregate in 12 patients. Extrinsic gastric compression was seen in 6 patients (splenic artery 4, left lobe liver 1 and anomalous spleen in 1 patient).

**Conclusion:** EUS is a useful tool in the evaluation of both benign and malignant gastrointestinal submucosal tumors. External gastric compression mimicking as submucosal lesion, as seen on upper endoscopy can also be readily distinguished by EUS.

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**Jejunostomy Tube Placement under Direct Visualization**

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**Purpose:** To evaluate a novel technique for percutaneous endoscopic jejunostomy tube (PEJ) placement under direct visualization.

**Methods:** A 35 kg pig was fasted for 48 hours prior to the surgery. This pig was intubated and sedated with general anesthesia. A pediatric colonoscope was passed to the proximal jejunum, and a location for the PEJ was marked based on transillumination and digital pressure. An opening in the jejunal wall was made using a gold probe. A Jagwire was then passed into the peritoneal space. A small incision was made in the abdominal wall with a scalpel, and a Kelly clamp was used to separate the fascia to facilitate insertion of the pediatric gastroscope into the peritoneal cavity. The pediatric colonoscope was used to visualize the transillumination from the pediatric gastroscope and direct its advancement to the location of the Jagwire. The Jagwire was then grasped by the pediatric gastroscope (via snare), and pulled out through the abdominal wall with the pediatric gastroscope. The pediatric colonoscope was removed and a 20 Fr PEG tube was tied to the Jagwire and pulled through the mouth and the upper gastrointestinal tract and then into position with the bumper pulling the jejunal wall tight against the abdominal wall. The pediatric colonoscope was then reintroduced and advanced to the PEJ site to confirm that the bumper was in good position.

**Results:** PEJ placement using the method described above was successful in a 35 kg pig. The jejunostomy tube was placed at 75 cm from the incisors, and the position was confirmed endoscopically after placement. The bumper was snug at 4 cm from the skin surface. There were no immediate complications. The pig was euthanized after the procedure.

**Conclusion:** A number of endoscopic techniques for PEJ placement are currently being studied. Unfortunately, direct PEJ placement has moderate or severe complications approximately 10% of the time. The use of T-fasteners to aid in PEJ placement is promising, but it still does not allow for direct visualization. We previously reported placement of PEJs in two 35 kg pigs under transgastric endoscopic guidance. However, PEJ placement using the novel technique described in this abstract allows for direct visualization while avoiding the need to create and then close a gastrotomy. Further research should focus on the refinement of the transabdominal instrument, and survival animal studies will be needed to demonstrate weight gain and monitor for leakage at the PEJ site.

Mean Procedural Times Grouped by BMI

	Exam Time	Cecal Int. Time	Procedure Time	Recovery Time
BMI < 20 N = 26	22.40 ± 7.05	11.65 ± 6.44	27.40 ± 7.43	39.77 ± 20.67
BMI 20–24 N = 200	20.68 ± 8.54	9.34 ± 5.30	25.45 ± 9.21	44.37 ± 22.77
BMI 25–29 N = 322	20.47 ± 9.37	8.73 ± 6.07	25.40 ± 10.61	44.87 ± 22.04
BMI 30–34 N = 132	20.64 ± 9.71	7.91 ± 5.40	25.70 ± 9.94	45.07 ± 28.16
BMI > 34 N = 44	21.70 ± 13.22	8.91 ± 6.89	27.38 ± 12.94	43.41 ± 20.01

1149

**Identifying Barriers To Keeping Endoscopy Appointments**

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**Purpose:** Missed appointments and procedures account for a significant burden to the healthcare system. Not only does it cause financial loss but it places constraints on already limited schedules. Estimates reveal an approximate no-show rate of 10% for most clinical situations. No studies have looked specifically at the experience in an endoscopy unit. The purpose of our study was to look at patient characteristics and reasons for not showing up for their endoscopic procedures.

**Methods:** Patient dates and times of missed procedures from our endoscopy suite were recorded over a three month period. A questionnaire was developed to look at demographics, healthcare history, and reasons for failure to make it to their appointment. Attempts were made to contact all of these patients by telephone within a few weeks of their visit. A patient that had their procedure from the same date and time of day was also contacted and information utilized as a control.

**Results:** Of 1,160 patients scheduled, 110 patients failed to show. 29 were reached and agreed to participate. The response rate equaled 26%. Our control group included 20 patients.

Patients more likely to miss their procedure were: female, on more than one medication, missed other appointments, seen in the emergency room more frequently, less likely to have had a Pap Smear, unemployed and disabled in their own opinion. All of these findings met statistical significance. Differences existed but were not significant for age greater than 66, number of medication allergies, distance traveled for procedure and presence of chronic illnesses. No difference existed in marital status, children at home, or having an annual mammogram. Missed procedures occurred most often on Tuesdays and in the mornings. Reasons given for failure-to-show included personal illness, death/illness of a family member and conflict in schedule.

**Conclusion:** Our study provides new insight on patients missing endoscopy procedures. Unlike other studies forgetfulness was not a prevalent reason for missing procedures. When asked how we could have helped them keep their appointment most patients stated it was unavoidable although a few indicated that better communication would have been beneficial. Studies have shown that simply just asking "is this time okay for you?" can improve attendance rates. Since personal and family illnesses cannot be predicted it can be difficult to fill all procedure times completely. Our endoscopy unit started scheduling one extra case per day to utilize any empty times due to failure to keep appointments.

1150

**Complications Requiring Hospitalization Following Primary Screening Colonoscopy**

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**Purpose:** To compare complication rates in outpatient colonoscopies performed for screening vs those performed for specific indications.

**Background:** Colonoscopy is the procedure of choice for Colon cancer screening in all individuals over the age of 50. Complications of colonoscopy have been described in the literature, but these studies have included colonoscopies performed for a variety of indications. Our aim was to determine if the complication rate for screening colonoscopy was similar to that of colonoscopies performed for other indications.

**Methods:** We retrospectively reviewed all patients undergoing outpatient colonoscopy at our institution from January 1, 1999 to April 1, 2006. Indications and findings of colonoscopy were recorded using the endoscopic database maintained by the Gastroenterology Division. The corporate database was used to verify if these patients were admitted to Henry Ford Hospital within 30 days of the procedure. The admission records of these patients were reviewed to verify if these admissions were related to compli-

cations of colonoscopy. Statistical analysis was performed using chi square analysis.

**Results:** 18,193 outpatient colonoscopies were performed during this period, of which 7344 were screening colonoscopies. There were 712 admissions within 30 days of colonoscopy. Of these, 59 were related to colonoscopy complications (3.7/1000), 19 of these were complications of screening colonoscopy (2.6/1000) ( $P = \text{NS}$ ). Most patients (88%) were admitted within one week of the colonoscopy. Complications for all colonoscopies included 36 bleeds, 11 perforations, 7 post-polypectomy syndrome and 5 miscellaneous. Bleeding was less common in patients undergoing screening colonoscopy 0.11% vs 0.26% ( $P = 0.026$ ). There was no statistically significant difference for other complications in screening colonoscopy patients. There was one mortality in the non-screening group. There was no significant association of complications with race, sex and type of bowel prep. Rate of complication was 3.1/1000 when a fellow performed the test and 2.9/1000 if performed by senior staff ( $P = \text{NS}$ ). Snare polypectomy was associated with a RR of 3.6 for all complications  $P < 0.001$ .

**Conclusion:** We found that the rate of complications requiring hospitalization following screening colonoscopy is not significantly different than colonoscopy performed for other indications at our institution. Snare polypectomy was associated with a higher rate of complications.

1151

**Endoscopic Ultrasonography Findings in Patients with Nonspecific Changes of the Pancreas on Computed Tomography: A Single-Center Experience**

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**Purpose:** To evaluate the efficacy of endoscopic ultrasound (EUS) in a cohort of patients with indeterminate pancreatic findings, such as "enlarged pancreas" or "prominent pancreas" reported on computerized tomography (CT) scan of the abdomen.

**Methods:** Retrospective single center study of 107 patients (56 males), who underwent EUS for further evaluation of inconclusive pancreatic findings on abdominal CT scan performed for various indications. Clinical data reviewed included: history of diabetes, alcoholism, weight loss; liver function tests; CBD diameter on CT scan, EUS and fine needle aspiration (FNA) cytology results.

**Results:** Mean age of the patients in the study was 61 years (range 26–88 yrs). 20 (19%) patients had diabetes, 19 (18%) had jaundice, 35 (33%) had significant weight loss, 20 (19%) had a history of alcoholism, and 34 (32%) had dilated CBD on the CT scan. After the upper abdominal EUS exam (with FNA whenever indicated) in these patients- 22 patients (21%) had adenocarcinoma of the pancreas, 14 (13%) had chronic pancreatitis, 28 (26%) had benign lesions, and 34 patients (32%) had a normal EUS exam. Pancreatic cancer was more likely to be found in patients with significant weight loss (OR-10.1; 95% CI: 3.3–30.60), jaundice (OR 9; 95% CI: 3–26.0), and CBD dilatation (OR 3.2; 95% CI: 1.25–8.5) by EUS in this cohort of patients with indeterminate CT scan findings.

**Conclusion:** EUS is an effective and safe modality for evaluating pancreatic lesions in patients with subtle abnormalities of the pancreas found on CT scan. Patients with jaundice, weight loss, and CBD dilatation are more likely to have underlying pancreatic cancer and should be referred early for EUS.

1152

**Upper Gastrointestinal Tract Lesion Identification by Small Bowel Capsule Endoscopy**

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**Purpose:** Previous studies have demonstrated capsule endoscopy's ability to identify lesions within the reach of conventional endoscopy. However, the significance of this has yet to be clarified, and at this time it is unclear in how much detail upper gastrointestinal images need to be reviewed for routine practice. The purpose of this retrospective review of capsule endoscopy findings is to determine frequency and significance of lesions in the upper gastrointestinal tract within the reach of conventional endoscopy.

**Methods:** A retrospective review was made of the Cleveland Clinic IRB approved Capsule Endoscopy Database consisting of 296 patients who underwent capsule endoscopy over a one year period at our institution. Significant lesion was defined as a lesion which explained the patient's clinical presentation. Arbitrarily we defined upper gastrointestinal as proximal to the ligament of treitz. Findings on capsule endoscopy were then compared to findings on upper endoscopy or push enteroscopy.

**Results:** Out of 296 patients, 77 patients with positive capsule endoscopy findings were identified (38 males, 39 females, mean age of 60.09 years). Of these 23/77 (30%) patients had significant findings on capsule endoscopy of upper gastrointestinal tract. The most common indications for capsule endoscopy were iron deficiency anemia (45%), gastrointestinal bleed (34%), and FAP (8%). Upper endoscopy and push enteroscopy findings were reviewed and were available for all 23 patients with significant findings in the upper gastrointestinal tract. 11/23 (47.8%) patients with positive capsule endoscopy had negative upper endoscopy or push enteroscopy. 12/23 (52.2%) patients with positive capsule endoscopy had corresponding positive findings identified on upper endoscopy or push enteroscopy. In 10/23 (43.5%) patients positive findings identified by upper endoscopy or push enteroscopy were not identified by capsule endoscopy.

**Conclusion:** Capsule endoscopy may be a useful diagnostic tool in identifying upper gastrointestinal lesions. This study showed that 47.8% of upper gastrointestinal lesions identified on capsule endoscopy was not seen on upper endoscopy or push enteroscopy. Although limitations of the study prevent defining recommendations, it is our opinion that upper gastrointestinal images in capsule endoscopy need to be reviewed as carefully as small bowel images.

## 1153

### Automated Video Capture for Quality Control during Colonoscopy: Real-Time Recognition of "Inside-the-Patient" Status

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**Purpose:** Automated, objective quality control during colonoscopy requires three key components: (1) automated digital video file generation, (2) automated metric extraction, and (3) automated report generation. Here we report on a novel, **real-time image analysis** technique that in completely automated fashion creates multiple digital video files each representing a single endoscopic procedure.

**Methods:** Two endoscopy rooms were equipped with video digitizers and PC-compatible workstations. Endoscopy image streams were digitized and forwarded to the workstations where during four days algorithms in real-time (analysis rate: 30 frames per sec) determined whether an image was "outside-the-patient" (OTP) or "inside-the-patient" (ITP; see figure). The algorithms are based on presence of specific color features and movement. If an ITP signal was detected, a digitized video file was created consisting of the first moment the endoscope was determined to be ITP until a status was reached of several minutes OTP. This approach allows for temporal removal of the endoscope for cleaning, polyp retrieval or combined procedures consisting of rectal stump and ileostomy inspection.

**Results:** Sixty-nine procedures were performed during the four days (see figure); all started with perianal or peristomal images and ended with sev-

eral minutes of OTP or no signal (equipment turned off). A few procedures were short (flexible sigmoidoscopy, ileoscopy or an aborted colonoscopy). A combined ileoscopy and rectal stump inspection was represented as a single procedure. Three additional small files were recorded: two test files in which the colon was simulated on purpose by introducing the endoscope into an enclosed fist and one (1/70; 1%) false positive result when the endoscope was left on in proximity of a material with skin color.

**Conclusion:** We successfully developed automated, real-time recognition of "inside-the-patient" endoscopy; our results form a first, important step towards **real-time quality control during colonoscopy**. [figure1]

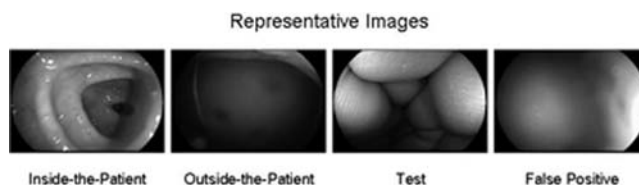


Table with Results

	Room 1			Room 2		
	Correct	Incorrect	Test	Correct	Incorrect	Test
Day 1	8	1	0	10	0	0
Day 2	9	0	0	9	0	0
Day 3	9	0	1	7	0	0
Day 4	9	0	1	8	0	0
	35	1	2	34	0	0

## 1154

### Utility of EUS-Guided Trucut Biopsy To Distinguish Pancreatic Rests from Gastrointestinal Stromal Tumors (A Case Series)

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**Purpose:** Although gastric pancreatic heterotopia or pancreatic rest (PR) is a harmless condition, it can be confused with other sub-epithelial tumors. Distinction based on the endoscopic ultrasound (EUS) appearance may be difficult if overlapping features are present. In these cases a histologic diagnosis is desirable. We describe our experience with EUS-guided trucut biopsy in 3 cases.

**Methods:** We identified three patients with a final diagnosis of gastric PR in whom EUS guided trucut biopsies were performed. The endosonographic features and histology findings were retrospectively reviewed.

**Results:** In all three patients EUS suggested involvement of the muscularis propria as typical for a gastrointestinal stromal tumor (GIST). All lesions were located in the gastric antrum, and the size of the lesions ranged from 14 mm × 10 mm to 15 mm × 11 mm. EUS-guided trucut biopsy was technically difficult in one patient due to extreme angulation of the endoscope tip, and no diagnostic specimen was obtained. Since a GIST was suspected, this patient underwent laparoscopic resection, which revealed the diagnosis of a PR. In the other two patients EUS-guided trucut biopsy enabled a histologic diagnosis and no further surveillance or intervention was recommended. No complications occurred.

**Conclusion:** Endoscopy and EUS appearances of a pancreatic rest can easily be confused with a GIST. EUS-guided trucut biopsy may enable a histological diagnosis which can prevent frequent surveillance endoscopies or surgery.

1155

**Irrigation Pump as an Aid to Colonoscopy**

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**Purpose:** Endoscopy irrigation pump is an aid to endoscopists which allows cleansing or lavage of the bowel. The pump can be operated by the endoscopist with a foot switch control without interrupting the procedure. It allows rapid cleansing of a site especially in a poorly prepared patient. The pump may also facilitate completion of a procedure that might otherwise be discontinued due to poor preparation. It enables the nurse to concentrate on other important functions like obtaining biopsies and assisting polypectomy. Accidental splashes that could occur with the biopsy channel flush can also be reduced. We wanted to investigate the effect of an irrigation pump on quality of bowel preparation, completion of procedure, procedure time and polyp detection.

**Methods:** We retrospectively reviewed colonoscopy data of patients over 15 day periods prior to and after introducing an irrigation pump at our endoscopy center. All patients received same instructions for bowel preparation and the same bowel preparation with Golytely and Dulcolax. Information collected included indication for colonoscopy, quality of bowel preparation, time for completion of procedure and findings on colonoscopy. Quality of bowel preparation was graded by the individual endoscopist using the Aronchick scale.

**Results:** Before introduction of irrigation pump (Group A) 103 patients underwent colonoscopy over a 15 day period and 104 after the irrigation pump (Group B). Both groups had similar number of patients for each indication for colonoscopy as well as for constipation and change in bowel habits. More patients in Group B had a good bowel preparation (40 vs 33) and more patients in Group A had fair bowel preparation (50 vs 43). Both groups had similar number of patients with poor (A/B: 16/17) and unsatisfactory (A/B: 4/4) bowel preparation. The endoscopist documented a need for repeat endoscopy for poor bowel preparation in 15 patients in Group A versus 8 patients in Group B. Both groups had same number of incomplete procedures (4) and terminal ileum intubations (17). Mean time for completion of procedure was significantly less in Group B (A/B:  $27.95 \pm 12.34$  vs  $23.36 \pm 11.08$ ,  $P$  value = 0.006). More patients in Group B had polyps though both groups were identical in indication for colonoscopy. The absolute number of polyps that were detected was greater in Group B (A/B: 167 vs 130).

**Conclusion:** Use of irrigation pump as an aid to endoscopy will improve a fair bowel preparation to make it good, will decrease endoscopy time and may improve polyp detection. This needs to be confirmed in a larger group of patients.

1156

**Safety Monitoring in a Phase I First-In-Human Study of the Anti-Viral Agent CMX001: A Novel Application of Wireless Capsule Endoscopy**

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**Purpose:** Wireless Capsule Endoscopy (WCE) is used to diagnose small bowel disease however it has been utilized infrequently as a method of evaluating drug induced small bowel (SB) mucosal changes in healthy adults. In preclinical studies the dose limiting toxicity of CMX001, a drug being developed to treat small pox, was enteropathy including small bowel involvement. The aim of this study was to utilize WCE to monitor and evaluate the effects of CMX001 on the SB mucosa for the purposes of determining the safety of the medication.

**Methods:** Healthy volunteers were pre-selected and divided into 6 person cohorts. Subjects with a history of significant GI disorders or recent NSAID use were excluded. Two of five planned cohorts have been enrolled and completed. In each cohort subjects were randomized to receive either a single dose of  $25\mu\text{g/kg}$  or  $50\mu\text{g/kg}$  CMX001 or a placebo in a 4(CMX001) to 2 (Placebo) ratio. The day prior to medication allocation each subject

underwent a baseline WCE. In preparation for the WCE, a clear liquid diet was instituted following lunch on the day before each study and overnight fasting was required. No bowel cleansing agents were administered. On the third day following medication administration WCE was repeated. All the WCE videos were evaluated twice by 2 separate readers; the readers were blinded to both study drug versus placebo and pre- versus post- drug exposure. Following WCE evaluation the results were paired by patient and the Lewis Score was added as a quantitative method of scoring the results.

**Results:** There were no significant interval changes in the SB findings between the pre- and post-dose WCEs. Several patients had pre-dose Lewis Scores that classified them as having existing mild inflammatory mucosal changes ( $< 134$ ). Findings were noted in all pre- and post- dose studies in patients who received either study drug or placebo. None of these patients experienced a post-dose worsening of their Lewis Score. Of the 24 separate WCE performed findings included, 33.3% with erosions, 62.5% had petechia, and 33.3% had erythematous/red spots. Other findings included denudation and mucosal irregularities.

**Conclusion:** In this on-going clinical pharmaceutical trial, the WCE has thus far successfully demonstrated the lack of clinically significant change in the SB mucosa of healthy volunteers ingesting a single dose of  $25\mu\text{g/kg}$  or  $50\mu\text{g/kg}$  CMX001.

1157

**The Effect of Small Bowel Transit Time on the Yield of Video Capsule Endoscopy**

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**Purpose:** Although the indications for capsule endoscopy (CE) continue to expand, it is not fully understood how the small bowel transit time (SBTT) affects the diagnostic yield of CE examination. Studies have shown that colonoscopy withdrawal time significantly affects the detection rate of colonic lesions: the faster the colonoscopy withdrawal time the lower the yield. We applied the same concept to CE, looking at the small bowel transit time (SBTT). Study aims: (1) To determine if increased duration of SBTT increases yield; (2) To assess the optimal SBTT that maximizes yield.

**Methods:** Between May 2003 and March 2007 a total of 412 patients underwent CE examination. All images were analyzed by an experienced team of gastroenterologists. In cases of uncertainty about any image there was a review by a second gastroenterologist before a consensus was reached. We collected data retrospectively from patient charts and electronic medical records. All 412 records were reviewed with 130 excluded based on defined study criteria. We classified the lesions found into positive finding group (PFG) and negative finding group (NFG). PFG represented any lesion types detected, e.g. bleeding, tumor, stricture, while NFG represented the absence of lesions.

**Results:** A total of 282 patients were included in the study. Mean age was  $64.5 \pm 15$  yrs, and 59% were females. The mean gastric emptying time (GET) and SBTT were  $34.4 \pm 35$  mins and  $239.9 \pm 78.6$  mins respectively. The yield was 50.7% with positive findings in 143 patients. The mean age was higher in the PFG compared to the NFG [ $66.5 \pm 14.8$  vs.  $62.5 \pm 15.1$ ,  $P$  0.026]. The mean SBTT in the PFG was higher than NFG but was not statistically significant ( $247.2 \pm 74$  vs.  $232.3 \pm 62.6$ ,  $P$  0.112). There was a trend of increasing yield with increasing duration of SBTT. There were more negative findings when the duration of SBTT was less than 200 minutes (45/81, 55.6%), but there was more positive findings when the SBTT was  $> 200$  mins (107/ 201, 53.2%) Yield by percentage in the PFG was lower than the NFG until the SBTT became greater than 200 minutes.

**Conclusion:** Increasing small bowel transit time augments the yield of capsule endoscopy. At SBTT greater than 200 minutes, more lesions are detected. Knowledge and utilization of optimal SBTT can enhance the effectiveness of CE examination of the small bowel. Newer agents need to be developed to slow down capsule transit time to increase the diagnostic yield.

1158

**Upper Gastrointestinal Findings in Hispanic Patients with Positive Fecal Occult Blood Test**

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**Purpose:** Upper GI evaluation in patients with positive fecal occult blood test (FOBT) and a negative colonoscopy has been justified in the presence of anemia and upper gastrointestinal (UGI) symptoms. However, it is not clear if asymptomatic or patients with colonic findings would benefit as well. The purpose of this study is to determine the role of upper endoscopy (EGD) in the evaluation of a positive FOBT.

**Methods:** From January 2000 to December 2005, we retrospectively reviewed the electronic medical records, endoscopic and pathology reports of Hispanic patients consulted to the VA Caribbean Healthcare System GI Service due to a positive FOBT. Those patients who had a colonoscopy and an EGD performed for this indication, no more than 90 days apart, were included in this study. Patients with history of gastrointestinal (GI) bleeding, colon cancer and inflammatory bowel disease were excluded. The statistical method use was Pearson Chi-Square and Odds Ratio.

**Results:** A total of 311 patients (97% men) with a mean age of 67 years (range 28–88) met the inclusion criteria. Sixty eight percent (212/311) of the patients had no reported upper GI symptoms. EGD was positive in 67% (207/311) of the patients. Findings included: erosive gastritis in 122/207(59%), duodenitis 71/207(34%), peptic ulcer disease 47/207(23%), erosive esophagitis 19/207(9%), angiodysplasias 13/207(6%), hypertensive gastropathy 11/207(5%), Barrett's 5/207(2.4%) and upper GI cancers 3/207(1.5%). NSAIDs and/or aspirin were used by 52% (163/311) of the patients. NSAIDs (N = 89) but not low dose aspirin use, had a significant association with UGI findings [OR 2; 95 CI (1.1–3.4);  $P < 0.02$ ]. The presence or absence of upper GI symptoms did not predict upper GI lesions ( $P < 0.21$ ). Colonoscopy findings did not influence the presence or absence of upper GI findings as well ( $P < 0.82$ ). Synchronous upper and lower GI lesions were present in 13% (40/311) of patients.

**Conclusion:** Upper endoscopy appears to play an important role in the evaluation of positive FOBT patients regardless of colonoscopy findings or the presence or absence of upper GI symptoms. The use of NSAID's is significantly associated with the presence of UGI lesions, increasing the yield of EGD. In this study, two thirds of our Hispanic patients had significant UGI findings including 1.5% incidental UGI malignancies. Large prospective studies and analysis of the cost effectiveness of this approach needs to be further evaluated.

1159

**Direct Endoscopic Placement of the Wireless pH Monitoring Device (The Bravo Capsule): A Novel Procedure**

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**Purpose:** The Bravo Capsule (pH sensor) is used for continuous wireless pH monitoring in the diagnosis of Gastroesophageal Reflux Disease (GERD). It is temporarily inserted into the esophagus and attached to the esophageal wall with the assistance of the Bravo delivery system. Initially an endoscope is used to determine the gastroesophageal junction distance. The endoscope is then removed and the device is placed blindly using the Bravo delivery system according to the measurements described by the endoscopy. After the placement of the Bravo capsule, the endoscope is reinserted again to confirm its attachment and location. This conventional method is a blind technique of placement and requires a second intubation of the esophagus to confirm attachment and correct positioning of the capsule.

The new technique used in the study of Bravo capsule placement provides an accurate positioning and confirms attachment of the capsule under direct endoscopic visualization. The Bravo delivery system is concurrently placed

without removing the endoscope and the device is released in the desired location.

This study was designed to evaluate a new technique of Bravo wireless pH device placement under direct endoscopic visualization.

**Methods:** After approval from the institutional review board (IRB), we conducted a retrospective study of 58 patients (29 patients with indirect and 29 patients with direct visualization) who had Bravo capsule placement between 2005 and 2007. The physician endoscopy procedure notes, nurse's notes, post procedure notes, and recovery notes were all reviewed. The 48 hour pH monitoring computer generated analysis results were also reviewed.

**Results:** Out of the 58 patients who had direct and indirect bravo capsule placement, there were no early detachments of the device and no immediate complications related to the procedure reported. There were no failures due to the technique in either the direct or indirect method.

**Conclusion:** There was no early detachment after the procedure from any patient in either the direct or indirect endoscopic placement techniques. The placement of the wireless pH monitoring device under direct endoscopic visualization provides a sufficient and a safe technique that negates the need for a second intubation. This also provides better confirmation of the attachment and positioning of the device. A larger prospective study would provide more information regarding complications and adverse effects.

1160

**Seizure-like Activity and Other Adverse Events While Using Propofol: A Retrospective Observational Study of 38,575 Sequential Endoscopies in an Outpatient Gastrointestinal Endoscopy Center**

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**Purpose:** To examine the occurrence of seizure-like activity and other adverse events during propofol-mediated gastrointestinal endoscopies.

**Background:** Propofol is a fast acting hypnotic, with action on GABA receptors. In recent years propofol has increasingly been administered for sedation during endoscopic procedures. Multiple studies have identified the propofol-related cardiopulmonary complications. More recently there have been case reports describing seizure like activity (SLA) in propofol-mediated sedation. However, reports of SLA during gastrointestinal endoscopy are scarce.

**Methods:** This is a retrospective observational study from a single outpatient practice comprised of 18 U.S. gastrointestinal endoscopists. Data was collected from January 2005 to May 2007. A total of 38,575 sequential endoscopic procedures were performed using propofol, administered by nurse anesthetists. Procedures included both, esophagogastroduodenoscopies and colonoscopies. ASA classes for patients undergoing endoscopy ranged from I-III. Standard monitoring with pulse oximetry, automated sphygmomanometry, and electrocardiographic telemetry was performed. All adverse events related to propofol administration were recorded.

**Results:** The number of propofol administered endoscopic procedures performed over a twenty-nine month period was 38,575, with a total of 107 (0.277%) anesthesia related complications. A total of 71 (0.18%) cardiopulmonary complications: 5 (0.013%) apnea/hypoxia, 23 (0.06%) possible aspirations, 11 (0.029%) laryngospasms, 2 (0.005%) hypotension 10 (0.026%) hypertension episodes, 17 (0.044%) arrhythmias, and 3 (0.0078% chest pain). SLA was identified in 1 (0.0026%) patient. A sample of 190 patients over a five-day consecutive period was evaluated to calculate the mean dose of propofol given during procedures. The mean dose of propofol was  $254 \pm 78$  mg (range of 60–600 mg). The one patient who had SLA received a total of 150 mg. The SLA occurred during induction with propofol, the patient remained conscious through the episode. Once resolved, the procedure was completed without further incident.

**Conclusion:** Propofol can be safely administered for gastrointestinal endoscopy. Seizure like activity is an extremely rare occurrence when utilizing propofol for sedation in patients undergoing gastrointestinal endoscopy, irrespective of dosage.

1161

### A Retrospective Comparison of Percutaneous Endoscopic and Radiologic Gastrostomy Tube Feeding

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**Purpose:** To compare efficacy and safety of percutaneous endoscopic gastrostomy (PEG) versus percutaneous radiologic gastrostomy (PRG).

**Methods:** A retrospective review of 70 health records evaluated: the indications for the procedure, technical success rate, complications during hospitalization (wound infections, bleeding, perforation, and death), length of hospital stay and death before discharge.

**Results:** 70 randomly selected patients with gastrostomies had a chart review: N = 30 for PEG and N = 40 for PRG. PEG patients had a mean age of  $71 \pm 15$  y; 56% were male. PRG patients had a mean age of  $67 \pm 18$  y; 63% were male. Major co-morbidities in the study population were: cardiac diseases 37%, pulmonary diseases 30%, hypertension 53%, diabetes 23% and neuromuscular diseases 77%. The mean length of hospitalization was  $35 \pm 27$  days. The indications for gastrostomy feeding were: 74% for neurological disorders, 18.6% for head and neck cancer; and 7.4% for dysphagia or other reasons. Technical success was similar for PEG and PRG groups (93.3% vs. 92.5%, respectively). Early complications occurred in 10% of PEG group vs. 12.5% PRG and ( $P = 0.633$ ). Two patients had GI bleed and required endoscopic intervention. 3 had bowel perforation and another 3 wound bleeding. Wound infection was more frequent in PEG group than PRG group (10% vs. 7.5% respectively;  $P = 0.711$ ). Late complications were more common in PRG group than PEG group (10% vs. 0%;  $P = 0.204$ ) including GI bleed in 2 patients, wound bleed in 1 and tube displacement in another. Incidental endoscopic abnormalities, an advantage of the endoscopic method, were identified in 9 patients (30%) of the PEG group. Seven had PUD; 1 had an esophageal ulcer, and another had a hiatus hernia. No procedure-related mortality occurred either group. 10% of the study group died for reasons other than the gastrostomy during the same hospital admission.

**Conclusion:** Percutaneous gastrostomy, whether placed endoscopically or radiologically, is a quite safe and effective method for enteral feeding. The radiologic method of insertion however had a modest increase in complications.

1162

### Should Patients Be Screened for Celiac Disease Prior to Gastric Bypass Surgery?

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**Purpose:** Obesity is the second leading cause of preventable death in the United States. It is estimated that there are 60 million obese people in the US. With obesity reaching epidemic proportions gastric bypass surgery has become an increasingly popular option for weight reduction. Therefore the question of screening patients prior to surgery has arisen. At this time no such screening criteria exists. Certain conditions such as the one presented in this case, celiac disease, may be detrimental in a patient who has undergone gastric bypass surgery.

**Results:** 57 year old obese Caucasian female who had gastric bypass surgery 6 months prior and presented with nausea, intermittent loose watery diarrhea, dull abdominal pain in the epigastric area for 2 weeks, iron deficiency anemia and laboratory values with evidence of malabsorption. Patient's post operative period was uneventful and she lost a total of 140 lbs since the operation. She underwent an upper endoscopy for evaluation which showed gastritis and enteritis. A small bowel biopsy was taken which showed lymphocytic duodenitis and mild atrophy of the villi compatible with celiac disease. Serologic studies were performed for endomysial IGA antibody and Gliadin IGG and IGA antibodies all of which came back positive. The patient was diagnosed with celiac disease and placed on a gluten free diet and proper nutritional supplementation. Subsequently her symptoms resolved.

**Conclusion:** This case clearly illustrates a patient with malabsorption due to celiac disease which was worsened by gastric bypass surgery. Therefore the question arises: should patients be screened for celiac disease prior to gastric bypass surgery. Further studies need to be performed to answer this question.

1163

### Biopsy Forceps-Guided Ileal Intubation (BIGII)

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**Purpose:** Majority of colonoscopies are done for screening for colon cancer in this country. However, there are still quite a number of colonoscopies done for diagnostic purposes, and in certain cases, ileal intubation is paramount for diagnostic work-ups. However, in certain situations, when the ileocecal valve is pointed southward and posteriorly, colonoscopic ileal intubation is impossible. The purpose of this study is to describe a new technique for the colonoscope to enter the terminal ileum in the cases of failed ileal intubation.

**Methods:** For the patients whom colonoscopic ileal intubation fails after 10 minutes of attempt, we would attempt to enter the terminal ileum with biopsy forceps-guided ileal intubation (BIGII) in 4 steps: 1) Tort the scope so that the ileocecal (IC) valve is at the lower quadrant; 2) Pass the biopsy forceps so that it passes beyond the IC valve. Turn the scope down so that the biopsy forceps is pressed against the IC valve; 3) withdraw the biopsy forceps slowly until the IC valve opening appears. Then slide the biopsy forceps into the terminal ileum (TI) as far as it meets resistance; 4) Gently push the scope into the TI as the biopsy forceps was withdrawn simultaneously in an one to one fashion.

**Results:** From December fifth to November 20, there were 1630 colonoscopies performed. 326 required ileal intubation for diagnostic purposes and 27 failed ileal intubation. The failure rate is 8.3%. The average age was 61.1 ranging from 23 to 86. There were 12 males and 15 females. Diarrhea(8), abdominal pain(8), anemia/GI bleed(7) and IBD(5) are the common indications for ileal intubation and only one has SBO. 24/27 (88.9%) were successful in ileal intubation by BIGII. And in most patients, the TI could be intubated by BIGII in three minutes. One patient who failed ileal intubation by BIGII was successful when the usual technique was attempted again.

**Conclusion:** BIGII is a very useful technique in intubating the terminal ileum and helping the diagnosis when the usual technique fails to intubate the terminal ileum.

1164

### Radiation Exposure in Endoscopic Retrograde Cholangiopancreatography

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**Purpose:** Present recommendations suggest limiting fetal irradiation to less than 500 mrem (0.5 rad) during gestation. From prior studies, the estimated fetal dose to pregnant patients undergoing endoscopic retrograde cholangiopancreatography (ERCP) who have been shielded with 0.5 mm lead aprons has been within acceptable safety guidelines. The radiation exposure to the pelvis from scattering of the x rays during ERCP is unknown. If the patients were pregnant but not aware, they would need to be counseled regarding the risk to the fetus following ERCP. To understand the level of skin exposure and so the estimated level of exposure to the fetus for better counseling, further studies are needed.

**Aim:** To determine the level of radiation exposure that occurs during ERCP to see if shielding of the abdomen is necessary for female patients of child-bearing age.

**Methods:** 5 prospective consecutive adult patients, (3 males and 2 non pregnant females) who were scheduled to undergo ERCP with or without pancreaticobiliary manometry were included in the study. Pre-procedure

preparation was done in a standard local protocol. The study was approved by local IRB, and all of the patients signed the informed consent. Prior to the ERCP, a calibrated lithium fluoride thermo luminescent dosimeter (TLD), (K&S Associates, Inc., Nashville, TN) were applied at four different sites, one in the suprapubic region anteriorly, two on right and left mid inguinal points respectively, and one over the sacrum. ERCP was performed for various indications with patients in prone position. Dosimeters were then removed and data was obtained on the level of radiation exposure. The results were then compared.

**Results:** A total of 5 prospective consecutive patients were studied. The average time of radiation exposure was 11.44 minutes (range 5.6–15.4 minutes). No adverse effects were reported secondary to the TLD. The average level of exposure was 0.625 rads (range 0.1 to 2.2). The approximate amount of radiation received at the center of pelvis is expected to be half of the dose recorded on the surface TLD, which appears to be in a safe range in pregnancy.

**Conclusion:** There is minimal radiation exposure to the unshielded abdomen and the pelvis during ERCP, far below the acceptable safety guidelines. Unshielded ERCP can be performed in a child bearing age female with or without known pregnancy with limited radiation exposure to the fetus.

## 1165

#### Endoscopic Treatment of Malignant Colonic Obstruction Using Expandable Metal Stents: Experience in 169 Patients

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**Purpose:** Self-expanding metal stent (SEMS) placement is a suitable therapeutic option for relief of colonic obstruction for both palliation and as “bridge to surgery.” This study aimed to investigate the efficacy of stent-based treatment for malignant large bowel obstruction.

**Methods:** From April 1999 to August 2006, we monitored patients who had undergone endoscopic placement of a SEMS for malignant colonic obstruction using a retrospective database. Enteral Wallstents and Ultraflex Precision Colonic stents (Boston Scientific) were used. Patients were characterized by age, malignant stricture location, stent-induced complications, and need for reinterventions.

**Results:** In total, 134 patients were treated (mean age 63.5 years, range 17 to 94) with palliative intent and 35 were treated as “bridge to surgery.” For 160 of 169 patients (94.7%), stents were placed successfully and obstruction clinically resolved in all but one of patient. The remaining nine patients experienced stent dislocation/dysfunction at the time of placement. The location of obstruction was: rectosigmoid colon (N = 97, 57.4%), descending colon (N = 24, 14.2%), splenic flexure (N = 11, 6.5%), transverse colon (N = 15, 8.9%), hepatic flexure (N = 9, 5.3%), and ascending colon (N = 13, 7.7%). There was no peri-interventional morbidity or mortality. One patient experienced an intra-procedural perforation. The median in situ time for the stents in the palliative group was 48.5 days (mean, 93 days) with 36 of 133 patients having complications (27.1%) including perforation (N = 12), occlusion (N = 12), migration (N = 8), erosion/ulcer (N = 3), and stent collapse (N = 1). Twenty-eight patients were treated endoscopically, and 36 underwent surgical intervention. Palliative patients had a median survival time of 167 days (range, 43 to 291). In the preoperative group, the median in situ time for the stents was 5.5 days (mean, 32 days). Three of the 35 preoperative patients had complications (8.6%) prior to operation (one occlusion, one migration, and one perforation). Of these patients, two required endoscopic reintervention. Overall, SEMS patients had an endoscopic reintervention rate of 17.8% and a surgical intervention rate of 21.3%. No further intervention was required for all remaining patients by follow-up.

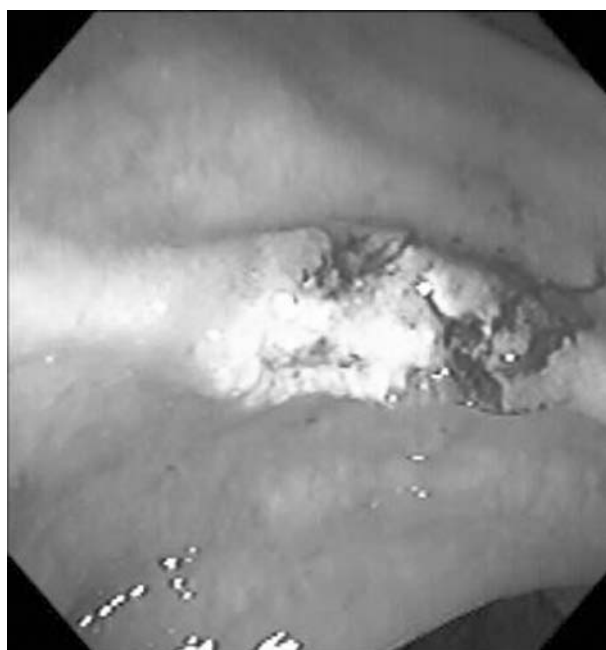
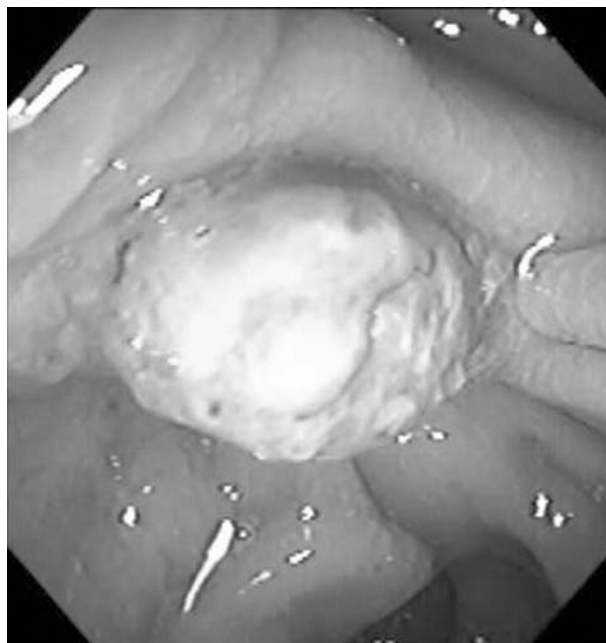
**Conclusion:** Endoscopic stenting can effectively relieve malignant colorectal obstruction as both palliative and preoperative therapy. SEMS can be applied to both left and right-sided colonic lesions with few complications.

## 1166

#### A Novel Use of Side-Viewing Endoscopy: Detection, Visualization, and Removal of Technically Difficult Left Sided Polyps

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**Purpose:** The traditional forward-viewing colonoscope provides a fairly complete view of the colonic mucosa, yet polyps located in areas of acute angulations and traversing folds have always been problematic to detect in the forward view. Moreover, the suboptimal visualization of these areas can make the excision of such polyps technically challenging. Here we describe a novel use for the side-viewing duodenoscope in detecting, visualizing, and removing technically difficult left-sided polyps around folds and turns in the colon.





**Results:** We report three patients who underwent colonoscopy for different clinical conditions who were found to have left-sided polyps in technically difficult positions with the traditional forward-viewing colonoscope. The side-viewing endoscope was inserted and advanced to the area where the polyp was located and proved to be better visualized (Fig. 1). The polyps were removed *en toto* through different techniques through the side-viewing endoscope providing unique angles of visualization and additional technical abilities to properly excise the polyp through the use of the elevator (Fig. 2). [figure1][figure2]

**Conclusion:** The use of side-viewing endoscopy for technically difficult polyps is a new application of an established instrument which should be considered when encountering these lesions.

## 1167

### Predicting Sedation Induced Respiratory Compromise during Colonoscopy

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**Purpose:** Predicting respiratory compromise during sedation for colonoscopies is beneficial as more patients are presenting with obstructive sleep apnea (OSA). Measurement of upper airway collapsibility (critical pressure of the pharynx,  $P_{crit}$ ) offers potential in assessing the propensity for sedatives to produce airway obstruction<sup>1,2</sup>. The specific aim for this study was to compare  $P_{crit}$  during sedation to the need for clinical intervention to maintain adequate ventilation.

**Methods:** We recruited patients who were scheduled for outpatient colonoscopy under intravenous sedation. Airway collapsibility was measured using a device to produce negative airway pressure and quantified in terms of the amount of pressure required to produce no inspiratory flow in spite of respiratory efforts. The comparison outcome measurement was a "clinical intervention score (CIS)" – a graded intervention performed by the nurse administering the sedation in order to restore adequate ventilation in the subjects.

**Results:** 17 patients (6 F), mean age 54 yrs (29–68), mean BMI 29 (23–40) completed the study. Sedation was managed by the gastroenterologist with midazolam, fentanyl or meperidine. No patients had a history of OSA, though three patients had an Epworth Sleepiness Scale score >10. Upper airway collapse (UAC) was elicited in 9/17 subjects. In 7/9 subjects, the  $P_{crit}$  was less negative during sedation than while awake (indicating more collapsible upper airways during sedation). Central apneas were elicited in 4 subjects who did not experience frank UAC, and 1 patient had a combination of central and obstructive apneas. 6/17 patients required a clinical intervention during their colonoscopies, though these were not predicted by their  $P_{crit}$  during sedation.

**Conclusion:** Sedation induced  $P_{crit}$  in our cohort did not predict the clinical intervention needed to restore adequate ventilation during sedation for colonoscopy. This contrasts with the correlation between  $P_{crit}$  under anesthesia with the patient's sleep apnea hypopnea index. Sedation may still maintain the pharyngeal tone that is abolished during anesthesia. Negative airway pressure application did elicit central apneas in our cohort, which may indicate instability of the central respiratory controller in the face of pharyngeal negative pressure reflex instigation.

Support: FAER Research Starter Grant.

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## 1168

### Recall of Informed Consent and Patient Satisfaction with the Addition of an Educational Video Prior to Colonoscopy

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**Purpose:** Obtaining informed consent prior to procedures is important for medico-legal reasons as well as for patient satisfaction. Studies have shown that patients often do not recall information about procedures. The purpose of this study was to evaluate whether the addition of an educational video to the standard informed consent process would improve recall and satisfaction of patients undergoing colonoscopy.

**Methods:** 100 patients were randomized to either standard consent (NVG) or standard consent plus an educational video (VG). Standard consent involved obtaining written and verbal consent. The educational video taped by an experienced endoscopist explaining the elements of informed consent was shown the day of the colonoscopy. It included the various indications, risks, benefits, and alternatives. Patients over 18, willing to participate were enrolled. All received a follow up phone call within 72 hours, at which time they were asked to recall the above elements of informed consent. We assessed spontaneous recall (SR), no recall, and satisfaction in both groups. 10 patients were lost to follow up and 45 were enrolled in each arm. Results were analyzed utilizing binomial distribution. A  $P$ -value of <0.05 was considered to be statistically significant.

**Results:** There was no significant difference in the demographic data between the groups. SR of the indications of gastrointestinal bleeding, anemia, abdominal pain, and change in bowel habits was statistically significant in favor of VG ( $P = 0.030, 0.044, 0.037, 0.0005$  respectively). SR of infection and perforation risks were significantly greater in the VG ( $P = 0.033, 0.010$  respectively). The VG demonstrated statistically significant SR of the benefit of removing colon polyps ( $P = 0.002$ ). Patients in the VG had significantly better SR of virtual colonoscopy ( $P = 0.0003$ ) and barium enema ( $P = 0.001$ ) as alternatives whereas the NVG had a significant lack of recall of the same alternatives ( $P = 0.001, 0.019$  respectively). The NVG had statistically significant lack of recall for the indication of anemia ( $P = 0.021$ ) and risk of infection ( $P = 0.003$ ). Level of satisfaction was significantly greater in the VG ( $P = 0.016$ ). A significant number of patients in the NVG compared to the VG, felt that the information provided was not enough ( $P = 0.016$ ).

**Conclusion:** The addition of an educational video prior to colonoscopy significantly improves recall of the elements of informed consent and patient satisfaction with their procedure.

## 1169

### Comparison of Direct Endoscopic Guided Placement of the Bravo Capsule with the Conventional Method

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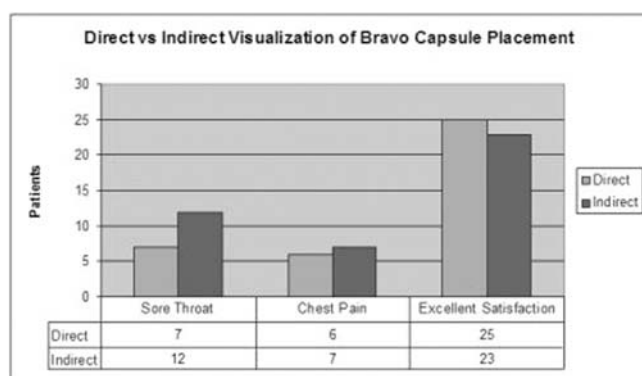
**Purpose:** The conventional method for Bravo placement used by the majority of gastroenterologists is a blind technique of placement and requires a second esophageal intubation to confirm attachment and correct positioning of the capsule.

The new technique presented in this study uses the Bravo delivery system without removing the endoscope and releases the capsule in the desired location under direct endoscopic visualization.

This Bravo capsule placement study compares adverse effects between the new direct endoscopic technique and the conventional indirect technique.

**Methods:** With institutional review board (IRB) approval, we conducted a post-procedural questionnaire of 58 patients (29 patients with indirect and 29 patients with direct visualization) who had Bravo capsule placement between 2005 and 2007. Patients were assessed by post-procedural symptoms including chest pain, sore throat, difficulty swallowing, and a satisfaction grade (1–10).

**Results:** Of the 58 patients who underwent Bravo capsule placement, 19 had a sore throat after the procedure (7 patients with direct endoscopic capsule placement compared to 12 with indirect capsule placement) ( $P = 0.26$ ). Thirteen patients had chest pain or chest discomfort following the procedure (6 patients with direct placement compared to 7 with indirect placement) ( $P = 1$ ). An excellent satisfaction grade (8–10) was noted by 25 patients from the direct endoscopy study and all 25 agreed to a repeat procedure if necessary as compared to 23 from the indirect endoscopy study ( $P = 0.73$ ). **Conclusion:** The placement of the Bravo wireless pH monitoring device under direct endoscopic visualization provides an effective and safe technique that negates the need for a second esophageal intubation. This also provides better confirmation of the attachment and positioning of the device. The incidence of sore throat in the direct method proved to be less common than that of the indirect method, however was not statistically significant. This can be attributed to a single esophageal intubation in direct endoscopic visualization versus reintubation in the indirect method, though a larger prospective study is warranted.[figure1]



## 1170

**Can Colonoscopy Performed for Reason Other Than Screening Replace Screening Colonoscopy for Colorectal Carcinoma Screening**  
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**Purpose:** Colonoscopy is performed as a screening procedure for colorectal cancer (CRC). During this procedure, polyps, which could be premalignant lesions, are removed thereby reducing the risk of development of CRC. Gastroenterologists also perform colonoscopy for other indications such as bleeding and anemia. The aim of this study is to determine if there is a difference in the rate of polyp detection between screening and other indications for colonoscopy.

**Methods:** All colonoscopies performed at Henry Ford Hospital for a period of one year between 03/01/1999 to 04/01/2000 were reviewed. The indication for colonoscopy and findings were noted in all cases. The primary end point was the detection of any polyp based on size and the secondary end point

was the detection of an adenomatous polyp. The chi-square test was used to calculate the percent differences in polyp detection between groups based on the indication for colonoscopy.

**Results:** There were a total of 2096 colonoscopies performed on 1547 patients. Of these patients, 48% were male, 67% were African American and 30% were Caucasian. Of the 2096 colonoscopies performed, polyps were detected in 980 (46.7%), and of these 675 (32%) were adenomatous polyps. Major indications for colonoscopy were screening (12%), surveillance (18%), abnormal radiology (4%), bleeding (30%), positive fecal occult blood test (17%), iron deficiency anemia (11%) and bowel habit change (7%). Rate of detection of any polyp, <10 mm polyp and adenomatous polyp are presented in Table-1. Rate of polyp detection (for all three groups) in screening and surveillance colonoscopy were higher in comparison with other indications and were statistically significant (except abnormal radiology).

**Conclusion:** The rate of detection of all polyps, including polyps <10 mm and adenomatous polyps, was significantly higher in screening and surveillance colonoscopy than other indications for colonoscopy. Any program using colonoscopy to screen for colo-rectal cancer that is based on bleeding or anemia has rates of polyp detection inferior to general screening and is inappropriate.

## 1171

**The "Jist" of It: Transgastric EUS-Guided Diagnosis of Small Bowel GIST Masquerading as a Peripancreatic Lymph Node**

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**Purpose:** A 76 y/o female with a history of coronary artery disease had an episode of mild pancreatitis managed conservatively. There was no biliary, toxic, or dyslipidemic etiology, and she denied jaundice, weight loss, diabetes, or steatorrhea. After a second episode 8 months later, a CT scan was acquired, revealing a cystic lesion in the body of the pancreas.

She was therefore referred for EUS. This showed a 17×8 mm anechoic lesion in the body of the pancreas with a thin wall and no septae. There was no associated mass, internal debris, or chronic pancreatitis, and both the common bile duct and pancreatic ducts were normal; FNA was performed. Incidentally noted was a 24×11 mm peripancreatic solid lesion resembling a lymph node (see image). A transgastric approach was then undertaken for both FNA and Trucut core biopsy.

The FNA of the cystic lesion stained positive for mucin, fluid CEA was 1637 ng/mL, and the cytology was negative, all consistent with a mucinous cystadenoma (MCA). The FNA of the peripancreatic mass was unrevealing, but the core biopsy had foci of spindle cells that stained positive for c-kit, strongly suggesting GIST.

The patient underwent an enucleation of the cystic lesion and a resection of a submucosal lesion in the fourth portion of the duodenum. Surgical pathology confirmed pancreatic MCA and small bowel GIST. In retrospect, the patient denied any bleeding or obstructive symptoms; review of the prior CT also failed to demonstrate any small bowel lesion.

This case highlights the discovery of a small bowel GIST found incidentally on endosonography due to the serendipitous location of the distal duodenal tumor immediately adjacent to the greater curvature of the stomach. GISTs

Table 1. Indication of colonoscopy and rate of polyp detection

Indication	Screening	Surveillance	Abnormal radiology	Bleeding	Postive FOBT	Iron deficiency anemia	Change in bowel habits
Rate of any polyp detection (%)	68	62	63	40	38	37	26
Rate of <10 mm polyp detection (%)	55	49	37	31	30	28	22
Rate of adenomatous polyp detection (%)	44	46	44	26	28	27	11

are relatively uncommon, with a prevalence of about 15/million, only 20% of which are found in the small bowel. The rate of malignancy is usually low, but in small bowel GIST, about 50% of lesions are malignant. They are classically subepithelial with central umbilication and positive immunohistochemistry for c-kit. The therapy for these tumors is resection if not metastatic; otherwise, tyrosine kinase inhibitors can be used.[figure1]



1172

### Successful Endoscopic Closure of Postoperative Colocolic Fistula

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**Purpose:** Colocolic fistula is a disabling complication of postoperative anastomotic colonic leak. Endoluminal closure may be an option worth pursuing in those who are not candidates for surgery.

**Aim:** We report endoscopic closure of a chronic colocolic fistula in a morbidly obese patient who was not a candidate for surgical revision.

**Case Report:** A 56-year old woman with morbid obesity (390 lbs) and sleep apnea underwent a right hemicolectomy for colon cancer. Her post operative course was complicated by a pulmonary embolism. Anastomotic leakage resulted in a large intra abdominal abscess that developed into a colocolic fistula (daily output: 50–100 cc fecal matter and pus). Due to morbid obesity and recent pulmonary embolism, surgery was deferred; endoscopic therapy was recommended.

**Endoscopic Therapy:** *Step 1:* Cap fitted colonoscopy allowed identification of a 1 cm fistula at the anastomotic site. *Step 2:* The fistula was probed with a forceps – small amount of pus came out. *Step 3:* Cautery of the fistula with a BICAP probe to freshen up the wound *Step 4:* Clip closure of fistula: 4 Resolution clips were used to close the defect.

**Follow-up:** *First 24 hours:* The fistula out put decreased from 50 cc to 2 cc within 24 hours. *3 month followup:* the fistula was found to be healed; intermittently, the scab broke down with discharge of a few cc of pus that required three courses of broad spectrum antibiotics. *6 months:* complete healing of fistula.

**Summary & Conclusion:** Our case demonstrates the feasibility of endoluminal closure of chronic colo-cutaneous fistula complicating anastomotic leak following colon resection. Endoscopic therapy resulted in a dramatic reduction of the fistula output from 50–100 cc to a few cc immediately after closure, with eventual closure of fistula after a few weeks. *In conclusion, endoscopic closure of colocolic fistula complicating anastomotic leak is an option worth pursuing.*[figure1]



1173

### Successful Ablation of Barrett Esophagus with Dysplasia Using the HALO Ablation System in a Prospective Cohort

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**Purpose:** To assess the safety and efficacy of a step-wise regimen of circumferential and focal ablation using the HALO ablation system (Barrx Medical Inc., Sunnyvale, CA) for the treatment of Barrett esophagus (BE) containing low-grade (LGD) or high-grade dysplasia (HGD).

**Methods:** HALO ablation system consists of a balloon based electrode array for circumferential and an endoscope -mounted, paddle-based electrode array for focal ablation of BE. Patients with BE and LGD or HGD, confirmed by 2 pathologists including 1 expert GI pathologists, were treated with circumferential ablation. Repeat ablation (circumferential or focal) was performed at 3 month intervals until BE was completely eradicated. Lugol's chromoendoscopy with targeted biopsies from visible BE and random biopsies from the original BE region were obtained at regular follow-up intervals to assess for residual intestinal metaplasia (IM) and dysplasia. A complete response (CR) is defined as all biopsies for a patient negative for any dysplasia, HGD, LGD or IM (separate analyses) at last follow-up. All adverse events were recorded.

**Results:** Sixty-four patients were treated, 62 had at least one set of biopsies post ablation and were included in the efficacy analyses (58 men; median age 71 years; median length of BE 5 cm; 39 LGD; 25 HGD, median follow-up 12 months). Results from the last biopsy follow-up of 38 LGD patients; 25 (68%) normal squamous mucosa, 8 (21%) focal islands of non-dysplastic IM, 1 (3%) IM indefinite for dysplasia, 2 (5%) LGD, and 1 (3%) HGD in the cardia. Results from the last available biopsy follow-up of 24 HGD patients; 13 (54%) normal squamous mucosa, 4 (17%) focal islands of non-dysplastic IM, 3 (13%) IM indefinite for dysplasia, 1 (4%) LGD, and 3 (12%) HGD. The CR for both LGD and HGD was 92% and 88%, respectively. A total of 64 patients were included in the safety analyses. 1 (2%) patient each had self-limited GI bleed and mild esophageal stricture. There have been no instances of subsquamous intestinal metaplasia, "buried Barrett," identified on review of >3000 biopsies.

**Conclusion:** Ablation of BE containing dysplasia using the HALO ablation system appears to be safe and effective, with CR for both LGD in the LGD cohort and HGD in the HGD cohort was 92% and 88%, respectively. Patient tolerance and safety with the procedure has been excellent. There has been no evidence of subsquamous intestinal metaplasia, "Buried Barrett" post-ablation.

1174

**What Questions Do Patients Ask during Colonoscopy? A Prospective Study in an Ambulatory Endoscopy Center**

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**Purpose:** Patient education prior to colonoscopy is important in facilitating compliance, reducing anxiety and establishing a better informed patient. Patient understanding of the procedure and what events will happen during the test are paramount in reducing stress driven reactions during the exam. We conducted a prospective study cataloging patient questions prior to and during conscious sedation to determine if current colonoscopy education pamphlets meet patient needs.

**Methods:** Consecutive patients undergoing colonoscopy in an ambulatory endoscopy center were enrolled. Age and sex demographics and indication for the procedure were recorded. Questions asked by patients were recorded during the procedure by nursing personnel.

**Results:** Study Duration: one week

Number of colonoscopies: 64

Age Range: 38–76

Median Age: 56

Modal Age: 46

Number of patients asking questions: 13

Indications for procedure: screening 12; change bowel movements: 1

Number of Questions Asked: 23

Categories of Questions and Percentage of Total Queries

Length of Procedure 17.4%

Interpretation of findings on Monitor 34.8%

Genitourinary query 4.3%

Medication questions 8.7%

Time to resumption of normal activities 4.3%

Administrative 4.3%

Queries regarding abdominal discomfort 8.7%

Queries regarding the colonoscope 4.3%

Limitations of examination 4.3%

Recovery time 8.7%

**Conclusion:** Patient questions during colonoscopy involved multiple topics that are not often addressed in colonoscopy education pamphlets. Inclusion of topics addressing explanation of images and artifacts on the endoscopy monitor, medications utilized, recovery time and limitations of the examination would be helpful in aiding patient education.

1175

**A Survey of the Practices of New York Area Endoscopists Regarding Colonoscopic Surveillance Intervals in Patients with Incomplete Bowel Preparation**

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**Purpose:** The purpose of the study was to conduct a survey of endoscopists in New York City area regarding their opinions about surveillance intervals for screening colonoscopy in patients with incomplete bowel preparation.

**Methods:** Approximately 300 surveys were mailed to NYC area gastroenterologists. Questions were asked regarding practice setting, involvement with trainees, the number of colonoscopies performed annually and the bowel prep used. Respondents were asked to define an “adequate prep.” Then they were given different scenarios of reasons for surveillance in patients with inadequate bowel prep, and asked when they would repeat the colonoscopy.

**Results:** Sixty five surveys were returned. Most respondents were in private practice (80%) and the majority performed 600–1000 colonoscopies per year. 73% of practitioners worked with fellows, of which 74% replied that they performed >50% of the colonoscopies themselves. 70% preferred to use a PEG solution while 30% used sodium phosphate based prep. 60%

of the endoscopists stated that they considered an adequate prep to be able to visualize >90% of the mucosa, while 32% accepted liquid stool which could be suctioned. The survey presented different scenarios of patients with incomplete preparations and asked about surveillance intervals. For an average risk patient with no polyp found, the majority would repeat before 3 years (26% in 1–3 years, 45% at or before one year). If the patient had an increased risk (i.e. family history of colon cancer), 58% would repeat before one year. If the patient had a prior tubular adenoma >1 cm, 30% would repeat in one year, and 42% before one year. If the patient had 1–3 tubular adenomas which were <5 mm found during the exam, 39% would repeat in one year, and 33% before one year. When asked how they would prepare the patient for the next exam, most preferred to use a “two-day” prep.

**Conclusion:** Colonoscopy remains the preferred method of colon cancer screening. Several guidelines have been published recommending surveillance intervals after initial screening colonoscopy. However, the guidelines do not address the question of how to manage the inadequately prepped patient. This study illustrates the wide variety of practices among endoscopists surveyed, and highlights the need for expert consensus opinion on how to manage the important and common dilemma of the incompletely prepped patient.

1176

**Endoscopic Detection of Duodenogastric Reflux Using Chromoendoscopy with Indigo Carmine**

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**Purpose:** Duodenogastric reflux (DGR) is risk factor for intestinal metaplasia (IM) of the stomach. IM is generally considered to be an early stage in the multi-step process leading to the development of gastric cancer or to be associated with an increased risk of gastric cancer. Detection of patients with DGR may be significant for follow up patients, but endoscopist can not always see reflux of bile during examination.

The aim of this prospective study was determination of the effectiveness of dye spray (indigo carmine) on detection of DGR during routine upper endoscopy.

**Methods:** In one institution, 55 patients (F20, M35; mean age 43) entered into a prospective study. Duodenal stenoses, acute pancreatitis, ileus and gastrointestinal bleeding were excluded. All endoscopic procedures were performed with video endoscopes by a single endoscopist. All stainings were performed during routine upper endoscopy after obtaining permission. We used to spray 10 ml 0,2% solution indigo carmine onto the mucosa in the second part of duodenum. Immediately after that, endoscope was removed from duodenum to stomach. During one minute we determined grade of dye's reflux.

**Results:** There was not reflux of indigo carmine in 43 patients, reflux until angle of stomach in 4, reflux to gastric body in 8 patients. In all patients, who had reflux until gastric body, there was abundance of bile in stomach. Pearson correlation coefficient between grade of dye's reflux and presence of bile in stomach was 0,94 ( $P < 0,001$ ). There were no complications after chromoendoscopy. Limitations: Small patient number and uni-centric study.

**Conclusion:** Here we present a new method of chromoendoscopy with indigo carmine. This new method is fast, easy and not expensive and can be used for visual detection of DGR.

**PEDIATRICS**

1177

**Use of CO<sub>2</sub> for Insufflation during Colonoscopy in Children**

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**Purpose:** To determine safety, tolerability and comfort of use of carbon dioxide for insufflation during colonoscopy in children.

**Methods:** After informed consent, a total of 84 consecutive patients undergoing colonoscopy were randomized to use either air or CO<sub>2</sub> insufflation. Ages ranged from 6 years to 16 years (mean 12). End tidal carbon dioxide was recorded before the examination, at 2 minute intervals during the examination and 10 minutes after it. General anesthesia was used for sedation in all cases. Pain at 5 and 15 minutes after the procedure was measured using a ten-point analog scale.

**Results:** Pain scores at 5 minutes after the examination were  $5.2 \pm 0.3$  for the air group and  $4.8 \pm 0.2$  for the CO<sub>2</sub> group (no significant difference). At 15 minutes the score were  $2.8 \pm 0.3$  for the air group and  $0.7 \pm 0.3$  for the CO<sub>2</sub> group (significant at  $P < 0.05$ ). End tidal CO<sub>2</sub> in both groups was no different.

**Conclusion:** Using CO<sub>2</sub> for insufflation during colonoscopy is safe and improves patient comfort. Patients who received CO<sub>2</sub> insufflation during their colonoscopy experienced less post-procedure discomfort. There was no evidence of CO<sub>2</sub> retention based on end tidal carbon dioxide monitoring.

## 1178

### Proof That Some Kids Really Do Like Their Vegetables: A New Flavor Option for PEG Solution

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**Purpose:** Polyethylene glycol (PEG) bowel preparations are commonly used prior to colonoscopy. Children often object to the taste of PEG due to the salty flavor and oily consistency of the solution. The aim of our study was to determine how mixing low sodium organic vegetable bouillon with Colyte would compare to unflavored and fruit flavored options.

**Methods:** A prospective IRB approved study of children ages 8–18 yrs was conducted in the Division of Pediatrics at the Cleveland Clinic. 100 children were enrolled and asked to taste 3 solutions: standard unflavored Colyte, cherry flavored Colyte and vegetable bouillon flavored Colyte. 1 oz servings of each solution were placed in unlabeled covered cups. The order in which they received each of the 3 cups was randomized. Each patient was asked to rate the taste of each solution on a 4 point scale and then identify the best and worst tasting flavor.

**Results:** For each flavor, the frequency and percentage of each ranking (best, middle, and worst) were calculated. In addition, frequencies and percentages of the rankings were calculated based upon the order in which the flavor was received and the flavor that was administered just prior to the flavor. The bouillon flavor was chosen as favorite by 55% of children (95% CI:44–66%). Cherry was the favorite of 30%, while the plain flavor was favored by 15%. The plain flavor was chosen as the worst flavor by 49%, while 27% and 24% found the cherry and bouillon flavor to be worst, respectively. Ignoring any potential effects of carryover and the ordering, there is a significant difference in the rankings of the flavors overall ( $P < 0.001$ ). Both the bouillon ( $P < 0.001$ ) and cherry ( $P = 0.004$ ) flavors were significantly better ranked than the plain flavor. However, a statistically significant difference between bouillon and cherry flavors was not observed.

**Conclusion:** All prior studies of bowel preparation flavoring have compared fruit flavors to each other or to unflavored solutions. This study is the first to evaluate the addition of bouillon flavor to the already salty and oily tasting PEG. Our study not only showed this to be a viable option but that children actually preferred low sodium organic vegetable bouillon over standard fruit flavoring. Bouillon flavoring of PEG has not previously been considered or studied in trials of patients undergoing bowel preparation. A large prospective trial studying the compliance and preparation outcome of this flavor option should be performed.

## 1179

### Impedance-pH Measuring in Preterm Infants with Apparently Life-Threatening Events

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**Purpose:** The aim of the study is to evaluate the diagnostic value of impedance-pH measuring in preterm infants with suspected ALTE (apparently life-threatening events).

**Methods:** Between December 2006 and April 2007, at the Paediatric Gastroenterology Unit of Parma, twenty-four-hour impedance-pH monitoring was performed in 14 preterm infants (3 male- 4 female), hospitalized at Neonatal Intensive Care Unit, University of Parma. The mean age of patients was 28 days with a range between 16–40 days. The MII-pH technique records changes in impedance to alternating current between electrodes caused by the passage of a bolus inside the oesophageal lumen and the changes in pH. A single-use combined MII/pH oesophageal probe, tested and calibrated before each examination, was inserted transnasally. The catheter was comprised of six electrode pairs measuring intraluminal impedance 2–3, 5–5–6, 5–8–9, 5 cm above the LES, and an antimony pH sensor 2 cm above the LES (Sandhill Scientific, Inc; Highlands Ranch, CO). An impedance amplifier delivers current with resulting current flow variations in response to intraluminal impedance changes. The data were stored in an ambulatory recorder and saved on a CompactFlash card.

**Results:** One study was excluded because of technical problems (total recording time 6 hours); a total of 13 infants represents the final patients included, all with a good tolerance of the study. The total recording time was  $23.4 \pm 1.5$  hours. The median time of the longest episode was 23 minutes (range 4–52 minutes). The median number of reflux events in 24 hours was 73 (range 38–119), with median number of acid reflux 37 (range 20–60) and of non-acid reflux 37 (range 11–62). The majority of reflux was only liquid (90%).

The median time of acid exposure of the proximal esophagus (distal channel of impedance probe) was 108 minutes (range 15–277 minutes).

**Conclusion:** Although more studies need to be executed, impedance-pH measuring seems to be a useful diagnostic procedure also in preterm infants. Our results showed that impedance-pH measuring is a useful and safe technique even in infants, although a normal value for children and infants has not been defined yet and more multicenter studies are necessary to better evaluate and analyze the results, such as the correlation symptoms/reflux.

## 1180

### Chromosomal 1p36 Deletion: Inflammatory Bowel Disease, Sclerosing Cholangitis and Annular Pancreas

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**Purpose:** Chromosome 1p36 deletion occurs in approximately 1 in 5,000–10,000 live births. It is associated with psychomotor retardation, oropharyngeal dysphagia, cardiac malformations, sensorineural hearing loss, debilitating seizures and cranio-facial dysmorphism. There has been one case report in the literature of annular pancreas with malrotation associated with 1p36 chromosomal deletion. There are no reports of sclerosing cholangitis or inflammatory bowel disease (IBD). We report a 15 month old male with chromosome 1p36 deletion who was referred for evaluation of persistent leakage of gastric contents from the G-tube site. In spite of acid suppression and changing the length and diameter of the gastrostomy tube he continued to have leakage. He also developed bloody diarrhea of non-infectious etiology and elevated liver functions. Esophagogastroduodenoscopy (EGD) revealed a generous duodenal bulb but the endoscope was easily advanced to the third portion of the duodenum. Upper gastrointestinal series (UGI) was normal. Colonic biopsies revealed cryptitis with no granulomas. Liver biopsy showed features of sclerosing cholangitis. He was started on steroids, 5-aminosalicylic acid and ursodiol with normalization of liver function tests and resolution of diarrhea. However, he continued to have formula leaking

from his G-tube site. UGI was repeated which showed nonobstructing narrowing in the second part of duodenum with dilated first part of duodenum consistent with an annular pancreas. During exploratory laparotomy for duodenoduodenoplasty, an intraoperative cholangiogram was obtained which showed beading of the extra hepatic ducts confirming the diagnosis of sclerosing cholangitis. His liver function tests remained normal on azathioprine and ursodiol. In spite of the duodenoduodenoplasty, he had ongoing G-tube drainage for which a feeding jejunostomy was placed.

**Conclusion:** To our knowledge, this is a first report of such association of IBD, PSC and annular pancreas in such a young age with chromosome 1p36 deletion.

## 1181

**Transient Neonatal Achalasia**

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**Purpose:** Neonatal achalasia is an uncommon entity in the newborn period that can present with feeding intolerance, vomiting and excessive salivation. We present two newborn infants diagnosed with achalasia after a subsequent work up of feeding intolerance.

The first patient was the only viable child after twin – twin transfusion delivered at 30 weeks. She was noted to have dysmorphic features and diagnosed with Cornelia De Lange syndrome. She was tolerating oral feedings until acute onset of vomiting and feeding intolerance at 6 weeks of age. Upper gastrointestinal series (UGI) showed narrowing of the distal esophagus with an associated dilatation of the proximal esophagus consistent with achalasia. Feedings were resumed through a nasogastric tube and an UGI was repeated in 3 weeks. Repeated radiological study showed normal gastroesophageal junction with no evidence of achalasia.

The second patient was a full term infant with unremarkable birth history. She presented with gagging, stridor and central cyanosis after her first several feedings. Upper GI study showed tapered lower esophagus with elongated narrow gastroesophageal channel and dilated, dystonic proximal esophagus compatible with diagnosis of achalasia. Nasogastric tube feedings were initiated and UGI was repeated in 1 week with significant improvement in the distal esophageal narrowing. Esophagogastroduodenoscopy showed no anatomic abnormalities with normal passage of the scope. She resumed oral feedings and had no subsequent feeding intolerance.

**Conclusion:** Both cases represent radiological presentation of neonatal achalasia that did not require further intervention which resolved over a short period of time. Transient achalasia or transient spasm of lower esophageal sphincter should be considered in infants with radiological findings suggestive of achalasia. Nasogastric tube feedings with subsequent reimaging of the esophagus should be attempted prior to conclusive diagnosis of achalasia.

## 1182

**Pneumatosis Intestinalis: Rare Presentation of Crohn's Disease Exacerbation**

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**Purpose:** Pneumatosis Intestinalis (PI) is a well recognized manifestation of necrotizing enterocolitis in neonates. Rarely seen beyond newborn period, PI has been reported in adults with connective tissue disorders, pulmonary, infectious and gastrointestinal diseases. We present a 15 year old girl with diagnosis of gastric Crohn's disease who developed sudden onset severe abdominal pain. She was diagnosed with Crohn's disease at 11 years of age and treated with steroids and 6-Mercaptopurine (6-MP). She was weaned of her medications after 2 years when she had normal histology on her endoscopic evaluation. Four years later, at the time of presentation, she was on acid-blocker treatment. She had severe right lower and right upper quadrant pain with no fever, diarrhea or vomiting. She had diffuse tenderness with

guarding and rebound. Her abdominal CAT scan showed multiple collections of intramural air within the walls of distal ileum and right colon. Because of persistent pain and rebound on exam, she underwent laparoscopic exploration. Blebs on the serosal surface of the terminal ileum were recognized as PI with no other abnormal finding requiring surgical intervention. She was started on steroids and immunomodulator therapy with resolution of her symptoms. There was no evidence of PI on repeated abdominal CAT scan in 2 weeks. She underwent endoscopic evaluation which showed active ileitis with normal colonic histology.

**Conclusion:** Although rare outside the neonatal period, PI can be a finding in patients with acute exacerbation of inflammatory bowel disease. In the absence of complications requiring surgical exploration, PI in a child with inflammatory bowel disease should be treated with anti-inflammatory therapy.

## 1183

**ABSTRACT WITHDRAWN**

## 1184

**Endomysial Antibody Testing Improves Sensitivity in Screening for Celiac Disease in Young Children; a Five Year Single Center Experience**

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**Purpose:** Screening for celiac disease (CD) is facilitated by sensitive (tissue transglutaminase {TTG}) and specific (endomysial antibody {EMA}) testing. At our institution, screening involves TTG and EMA testing. Our aim was to analyze the use of serologic testing for CD at our children's hospital

over the past five years to characterize use patterns and to determine the utility of EMA testing.

**Methods:** Retrospective review of celiac panels performed at CHOP between 1/02 and 3/07 was performed to identify all TTG and EMA IgA testing. Electronic medical records were reviewed and clinical information and results of statistical analyses are summarized in tables below.

**Results:** Overall, 9746 celiac panels were performed in 5890 patients, with 5.7% of patients displaying TTG positivity and 3.8% displaying EMA positivity. Data is analyzed by year and displayed in table below. The mean TTG value in TTG+/EMA- discordant patients ( $30 \pm 17$ ) was significantly lower than TTG+/EMA+ patients ( $214 \pm 252$ )  $P < 0.001$ . TTG-/EMA+ patients were significantly younger ( $8.8 \pm 4.8$  yrs) than TTG+/EMA+ ( $11.5 \pm 4.0$ ) and TTG-/EMA- patients ( $11.4 \pm 3.6$ )  $P < 0.01$ . Further analysis revealed a higher rate of TTG-/EMA+ results in 0–4 year old children versus 5–20 year old children.

	Seropositivity by year					
	2002	2003	2004	2005	2006	2007 (3 mos)
Celiac panels	380	728	1141	1549	1635	451
TTG Positive %	6.58	5.91	4.38	4.91	6.61	5.54
EMA Positive %	3.42	3.02	3.24	4.26	3.97	4.00

	TTG-/EMA+ Results by Age Group		
	0–4 Years Age	5–20 Years Age	P value
TTG-/EMA+ in All Patients	3.10%	0.40%	0.013
TTG-/EMA+ in TTG- Patients	3.20%	1.00%	0.047

**Conclusion:** No major change in positivity rate was observed in the past five years. Not surprisingly, EMA displayed a low sensitivity of 68%, with greater sensitivity seen in higher TTG values. However, in 3.2% of patients, EMA testing was positive in the face of negative TTG testing, particularly in younger children. Despite the extra cost and subjectivity associated with EMA testing, it may improve sensitivity when screening a young child.

## 1185

### Prevalence of Gastroesophageal Reflux in Children Aged 2–15 Years Old with Chronic Abdominal Pain: 9 Years Experience

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**Purpose:** Gastroesophageal reflux (GER) is one of the most frequent clinical disorders affecting the gastrointestinal tract of infants and children and chronic abdominal pain is one of the hallmarks of this disease. The purpose of this study was to find the prevalence of GER in children with chronic abdominal pain that needed esophagogastroduodenoscopy (EGD) for final diagnosis.

**Methods:** All children aged 2–15 years old suffering from chronic abdominal pain that underwent EGD by the author in the only pediatrics gastroenterology ward in south-western of Iran were reviewed and enrolled in this study. The data obtained from the patients files which are kept in the hospital's archive.

**Results:** During 9 years(1998–2007) totally 1156 patients (599 boys, 557 girls) aged 1.5 months to 15 years with different upper GI tract problems underwent EGD in the gastrointestinal ward of Aboozar Children's Hospital, Jundishapour University of Medical Sciences. There were 804 (69.5%) patients (416 boys, 388 girls) older than 2 years who enrolled in our study. Among this age group, we found 449 cases (239 boys, 210 girls) with chronic abdominal pain needed EGD. When the procedure was performed, the diagnosis of esophagitis due to GER was suspected in 86(19%) patients (49

boy-37 girl) by observing obliteration of the Z- line and was confirmed by histopathological changes in esophageal biopsies. There were 8 cases with Barrett's esophagus all aged more than 6 years with history of suspicious symptoms of GER in infancy and later on. Treatment with prokinetic drugs and PPI or H2 receptor blockers was undertaken. Successful treatment was observed in 96% of all patients 6 months after treatment was initiated and on follow up. Surgical antireflux procedure was performed to patients with no resolution of symptoms after 6 months of therapy.

**Conclusion:** In conclusion, GER in children with chronic abdominal pain beyond infancy is not rare and tends to be chronic and severe and such patients are at high risk of developing serious complications without early diagnosis and treatment.

## 1186

### Use of Rifaximin in Pediatric Patients with Inflammatory Bowel Disease

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**Purpose:** Rifaximin is an antimicrobial approved by the U.S. FDA in 2004. It has poor systemic absorption and *in vitro* activity against enteric Gram-positive and Gram-negative bacteria making it a reasonable option for GI infections. Adult studies that have been done show promising results evaluating the efficacy of Rifaximin for use in inflammatory bowel disease (IBD). Our aim was to determine if Rifaximin is an option for use in pediatric patients with IBD.

**Methods:** A retrospective IRB approved study of 23 children ages 8–21 yrs was conducted at the Cleveland Clinic in patients with known diagnosis of IBD. We collected data including the time of diagnosis, extent of disease involvement, previous treatments, more recent treatments and current symptoms. While on Rifaximin, symptom improvement and lag to improvement were evaluated.

**Results:** Review of the data revealed that of the 23 patients, 12 had Crohn's and 11 had Ulcerative Colitis with a mean age of 15.08 yrs. The most common complaints were diarrhea (87%), abdominal pain (74%) and bloody stools (65%). Of the 23 patients that were prescribed Rifaximin only 3 were prescribed concurrent steroids. Patients were given Rifaximin at varying doses from 400 mg to 1200 mg per day. Analysis revealed that of the 20 patients that presented with diarrhea 16 had relief of diarrhea within 4 weeks of treatment, 5 within 1 week of starting Rifaximin. In 17 patients that presented with abdominal pain, 12 patients had relief within 4 weeks, 3 of these patients had relief within 1 week. Visible bleeding resolved in 10 of 15 patients within 4 weeks of therapy, 3 of the 10 had improvement within 1 week. Only one patient had a negative side effect of temporary increase in diarrhea symptoms upon starting the Rifaximin.

**Conclusion:** Rifaximin was well tolerated in our pediatric patients with IBD and showed favorable results. No serious adverse events occurred. Larger prospective studies with standardized dosages are needed to evaluate efficacy and determine optimal dosing of Rifaximin in this population.

## 1187

### Utilization of Nitazoxanide for the Empiric Treatment of Pediatric Diarrhea of Unknown Etiology

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**Purpose:** Diarrhea of unknown etiology is a common reason a pediatric patient seeks presents to the office. While there are many reasons pediatric patients develop diarrhea, microbial insult has been targeted as a major contributor to this disease. Parasites, bacteria, and viruses are part of the spectrum of implicated organisms. Since testing for a specified organism

is often inconclusive, untimely and costly, clinicians often prescribe a trial of empiric antibiotics. Nitazoxanide (NTZ) is a first in class thiazolide antibiotic, first indicated in pediatrics, with activity against anaerobic bacteria, protozoans, helminthes, and gastrointestinal viruses. Furthermore, NTZ has a placebo-like safety profile, high gastrointestinal (GI) concentration, and has limited to no activity against probiotic species. The purpose of this review is to evaluate the effectiveness of NTZ as empiric therapy for the treatment of diarrhea of unknown etiology in pediatric patients.

**Methods:** A chart review was performed on all patients treated with NTZ from February 2006 to May 2007 with complaints of generalized diarrhea not attributed to any cause, including suspected small intestinal bacterial overgrowth (SIBO) or *Clostridium difficile* associated diarrhea (CDAD). Efficacy was measured as resolution of the patient's diarrhea and resolution of chief complaints by the end of therapy. Patients returned to the office 3–6 weeks post treatment for follow-up.

**Results:** Four patients were treated with NTZ for diarrhea of unknown etiology in this time period. The range of NTZ doses used was 200 mg – 500 mg BID for 3–10 days, mean total dose and duration was 700 mg/d for 6 days. Overall 4/4 patients reported resolution of diarrhea and normalization of stools as well as resolution of primary complaints (abdominal pain, nausea, epigastric tenderness) that were present upon initial examination. No clinically significant adverse reactions attributable to NTZ were identified during the study.

**Conclusion:** Nitazoxanide appears to be a safe and effective therapy for the empiric treatment of diarrhea of unknown etiology in pediatric patients. Larger controlled clinical trials are warranted to support these findings.

## 1188

### Pediatric Patients Have Shorter Lansoprazole Half-Life Than Previously Reported

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**Purpose:** Traditional pharmacokinetic teaching suggests that the elimination rate (half-life) of drugs is related to patient age. However, the package insert for lansoprazole, a common proton-pump inhibitor (PPI) drug, reports that its "pharmacokinetics in pediatric patients aged 1 to 17 years [are] similar to those observed in healthy adult subjects." Numerous recent articles, in contrast, suggest that higher dosages are needed for children, although these articles establish no definite pharmacokinetic relationship between patient age and drug half-life. Establishing the correct half-life is important for appropriate dosage regimen development for PPI drugs.

**Methods:** Evaluation of previously published literature reveals an unusually large degree of variability in most studies. This variation can be caused by: (1) rapid versus slow metabolizer status based on genetic variation in Cytochrome P450, (2) immature hepatic function, (3) hepatic dysfunction,

and (4) errors related to timing of blood draws with enteric-coated products. Meanwhile, when the ages of the patients in the same studies are plotted against the respective half-lives of lansoprazole, an increase in half-life with age is observable. After removing data involving patients with immature hepatic function and eliminating outlying points by using statistically acceptable methods, the relationship between age and half-life becomes even more evident.

To further investigate this relationship between age and half-life, a single dose of buffered lansoprazole suspension was administered to six children and pharmacokinetics were evaluated by standard methods. The drug was delivered in caracream, a flavored suspension that is buffered with sodium bicarbonate (which causes immediate release of lansoprazole into the bloodstream and, therefore, the elimination phase is discrete from the absorption phase and timing of blood draws is much simpler).

**Results:** The half-life of the drug in each of the six patients was much lower than in other studies involving adults; furthermore, almost no variability was evident. When this data is compared with previously published data in pediatrics, it becomes clear that lansoprazole half-life increases with age.

**Conclusion:** These results explain why many clinicians find a need for larger daily doses of PPIs in children and the consideration of such factors is critical in the effort to control Gastroesophageal Reflux Disease in children.

## 1189

### pH Probe Indices in Infants with Gastroesophageal Reflux Presenting with or without Respiratory Symptoms

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**Purpose:** There is little data available about GER in proximal esophagus of infants with and without respiratory symptoms (RS). We compared reflux indices (RI) in proximal channel (PC) and distal channel (DC) of infants suspected to have GER with or without RS to the previously published normal values (Bogucka).

**Methods:** Retrospective review of RI in infants with suspected GER who were admitted to Loma Linda Children's Hospital and underwent Medtronic(R) dual-channel EpHM (sensors spaced 5 cm apart) between 1/1/2005 and 12/31/2005. RI in PC and DC of these infants was then compared to previously published normal RI values.

**Results:** There were 82 infants (age range 2 weeks to 12 months) who underwent EpHM during the study period. Of these, 41 had RS such as cough, wheezing and gagging (Group 1) while the other 41 had non-respiratory manifestations of GER such as feeding disorder, failure to thrive, spitting or vomiting (Group 2). Data was analyzed using a 2-tailed Pearson's Correlation.

**Conclusion:** 1. RI in PC and DC are correlated irrespective of presence or absence of RS. 2. Esophageal clearance time is delayed in infants with GER and (+)RS. 3. Abnormal esophageal motility may be the underlying mechanism of GER with (+)RS.

Reflux Index	(+) Respiratory Symptoms*	(-) Respiratory Symptoms*	Reference Normal RI values***
PC Total Number of Reflux Episodes	12.9 ± 15.2	13.5 ± 18.2	24.32 ± 24.92
PC Fraction of Time pH<4 (%)	3.4 ± 4.1	3.4 ± 4.9	0.87 ± 1.01
PC Number of Long Reflux Episodes (>3 min)	1.4 ± 2.4	1.4 ± 2.5	0.31 ± 1.15
PC Duration of Longest Reflux (min)	7.9 ± 9.1	6.4 ± 13.0	2.72 ± 3.51
PC Esophageal Clearance Time (min/episode)	2.7 ± 1.4 **	2.1 ± 2.2	0.44 ± 0.67
DC Total Number of Reflux Episodes	23.6 ± 21.1	26.4 ± 28.0	49.51 ± 34.88
DC Fraction of Time pH<4 (%)	6.2 ± 6.4	7.7 ± 10.4	2.19 ± 1.43
DC Number of Long Reflux Episodes (>3 min)	2.3 ± 2.9	3.2 ± 5.2	0.7 ± 0.89
DC Duration of Longest Reflux (min)	13.0 ± 18.9	13.5 ± 19.2	6.08 ± 5.58
DC Esophageal Clearance Time (min/episode)	2.7 ± 1.1 **	3.2 ± 2.0	0.57 ± 0.37

\*There are no significant differences between any of the tested variables between children with or without RS manifestations of GER. \*\*Esophageal clearance time in PC as well as DC of children with GER and (+)RS was significantly different from normal reference RI values ( $P < 0.05$ ). \*\*\*Bogucka, J. Pediatric Gastroenterology and Nutrition 31:3, 2000



1190

### Pneumatic Dilatation with a 35 mm Balloon, a Safe and Effective Initial Therapy in Pediatric Achalasia

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**Purpose:** Achalasia is a progressive, incurable and rare disorder of esophageal motility characterized by aperistalsis and incomplete relaxation of the lower esophageal sphincter (LES) in response to swallow. Functional obstruction created by the poorly functioning LES is thought to be the cause of symptoms. Current therapies aim to reduce the distal esophageal obstruction. Pneumatic dilation (PD) use is well established in adults. However, many patients require repeat dilations to achieve resolution of symptoms. A number of factors, including young age, have been associated with poor outcome. Only few studies describe successful PD in children. We report a series of pediatric patients with achalasia initially treated with PD using a 35 mm Rigiflex II balloon dilator.

**Methods:** We report five consecutive patients, ages 13 to 18 years, diagnosed with achalasia at The Children's Hospital at Montefiore between July 2006 and October 2006, who underwent PD. Duration of symptoms prior to presentation ranged from 2 months to 5 years. All patients met the esophageal manometric criteria for achalasia. Follow-up period ranged from 4 to 7 months post dilation. Patients underwent a single esophageal PD using a 35 mm Rigiflex II achalasia balloon dilator. The dilator was passed over a guidewire and positioned at the level of the gastroesophageal junction under fluoroscopic guidance. The balloon was rapidly inflated to achieve complete effacement of the waist. The inflation was maintained for 2 minutes. The balloon was then deflated and removed. An endoscopy was performed to evaluate the gastroesophageal junction. A water soluble contrast study was obtained to evaluate for perforation. Procedures were performed under general anesthesia. Patients were observed overnight.

**Results:** Patients reported complete resolution of achalasia related symptoms 1 to 2 weeks after the procedure. There were no complications during the procedures or in the immediate post-dilation period. At 1 month follow-up visit one patient reported symptoms of gastroesophageal reflux. All patients were asymptomatic at the most recent visit, 4 to 7 month post-procedure.

**Conclusion:** In our patients, a single PD with a 35 mm balloon used as initial therapy was safe and effective in the management of pediatric achalasia. We speculate that using a large size balloon for the initial dilation in children with achalasia minimized treatment failure related to greater esophageal wall pliability noted in young patients.

1191

### Demographic Profile of Children Diagnosed with Celiac Disease

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**Purpose:** To study the demographic profile of children with Celiac Disease (CD) diagnosed at a tertiary referral center in the Midwest.

**Methods:** Retrospective review of institutional database for all cases that fulfilled the diagnostic criteria of CD during a 5 year period (2002–2007): duodenal histology consistent with CD (Marsh criteria) and/or positive serology (tissue transglutaminase, endomysial antibodies).

**Results:** A total of 120 children (13 months to 18 years; mean 7 years) were diagnosed with CD. 22 (18%) were below 2 years. There were 50 males and 70 females. Presenting symptoms were growth failure (35%), diarrhea (29%), constipation (13%), anemia (6%), asymptomatic (17%). Comorbid conditions included immunologic disorder (26%: IgA deficiency 12, IDDM 7, eosinophilic esophagitis 4, IgG2 deficiency 1, lupus 1, juvenile dermatomyositis 1), genetic disorders (19%: Down Syndrome 17, Turner Syndrome 1, chromosomal deletion 1), and developmental/behavioral disorders (6%: Autism 1, Asperger syndrome 1, Tourette syndrome 1, ADHD 2, Apraxia 1).

Family history was positive in 23% subjects (mother 8%, sibling 4%, father 3%). Endoscopic biopsies were performed in 99 of 120 subjects (82%) and were positive in 85 (86%). All of the 14 subjects with normal biopsies had positive serologies.

**Conclusion:** Younger age at diagnosis of CD at our center most likely reflects early recognition of risk factors (immunologic, genetic and developmental/behavioral disorders) and screening. A higher prevalence of CD in females and in mothers is a novel observation of this study.

1192

### The Constipated Child: Is There a Correlation between Symptoms and Manometric Findings?

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**Purpose:** The aim of our study was to evaluate symptoms in chronically constipated children undergoing anorectal manometry and determine if any correlation exists with manometric variables.

**Methods:** 123 patients were prospectively enrolled and completed symptom questionnaires. Anorectal manometry was performed per standard protocol.

**Results:** Of the 123 patients enrolled in the study 57.7% were male. Patient age ranged from 0.2 to 17.8 years, and the mean age was 7.5 years. The average duration of constipation was 4.84 years. The average number of stools per week was 3.6. Average time spent in the defecation process was 13.3 minutes. The incidence of hematochezia was 30%. Delayed passage of meconium was reported in 45 of 99 patients (45.5%). Significant correlation was found between frequency of soiling and threshold for Recto-Anal Inhibitory Reflex (RAIR) ( $P = 0.029$ ). The volume of first urge was also positively correlated with frequency of soiling ( $P = 0.034$ ). There was significant correlation of withholding behavior and the maximum volume tolerated ( $P = 0.020$ ). The presence of blood was inversely correlated with the maximum volume tolerated ( $P = 0.004$ ). No correlation was found between severity of complaints and the presence of paradoxical puborectalis contraction, and 90.5% of patients did have paradoxical puborectalis contraction.

**Conclusion:** Anorectal manometry continues to provide additional new information and assist in managing patients with this very common chronic pediatric affliction. Based on our findings we recommend increased sitting times for scheduled toileting, and additional attention should be paid to patients with delayed passage of meconium.

1193

### Spectrum of Hepatitis B Infection in Children: Report of 167 Cases from a Developing Country

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**Purpose:** Information regarding the various manifestations of hepatitis B infection in children from developing countries is scanty. We have studied the clinical, biochemical and serological aspects of hepatitis B infection in children.

**Methods:** From January 1998 to May 2007, 167 children (up to 14 years of age) presented with hepatitis B infection to our tertiary care hospital, were studied. Their clinical, biochemical and serological details were recorded in a proforma. Depending upon the serological pattern, the children were classified into acute hepatitis B or AHB (HBsAg & IgM anti HBc positive), chronic hepatitis B or CHB (HBsAg positivity for more than 6 months). The latter group was further subdivided into three; inactive HBsAg carrier (HBsAg, anti HBe positivity & HBeAg negative with ALT < 2 times upper limit of normal [ULN]), replicating virus with activity (HBsAg and HBeAg positive and anti HBe negative with ALT > 2 times ULN), and replicating

virus without activity or immune tolerance phase (HBsAg, HBeAg positive and anti HBe negative with ALT <2 times ULN).

**Results:** The mean age was  $8.5 \pm 3.8$  years and 146 of them were male. The proportion of AHB and CHB was 37% & 67% respectively. The source of infection in the majority of AHB was intramuscular injection (53%) & 95% became HBsAg negative after 6 months. Of the 105 CHB children, 76% were incidentally detected and 24% were symptomatic (2% HCC and 22% CLD). Of the 80 incidentally detected children, 37.5% had inactive hepatitis B, 37.5% had replicating HBV without activity and just 25% had replicating HBV with activity. The majority of mothers (61%) of children with immune tolerance phase infection were positive for HBsAg. We managed to give interferon therapy in 20 children and 10 of them (50%) had responded (e-antigen seroconversion). Overall, 9 children died (7 of 10 FHF, and two CLD).

**Conclusion:** In developing countries, almost one third of HBV infections are acute and intramuscular injection is a common source. Like in adults, 95% children too clear HBsAg after an attack of AHB. The majority of CHB in children are incidentally detected and a major portion is perinatally acquired and in immune tolerance phase.

## COLORECTAL CANCER PREVENTION

1194

### Outcomes and Complications in Average Risk Colon Cancer Screening in a Community Hospital

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**Purpose:** To evaluate the outcomes and complications of average risk screening for colon cancer when done in a community hospital setting.

**Methods:** Between March 2002 and March 2007, all colonoscopies performed by the study endoscopists were entered into a database. Completeness of exam, adenoma detection rate, cancer detection rate, and significant complications were recorded. Cancer staging was ascertained from the pathological record.

**Results:** Of the 15,228 colonoscopies done during this period, 3968 (46% M, 54% F) were done for average risk screening. The age range for those screened was 40–49(.2%), 50–59(37%), 60–69(32%), 70–79(26%) and 80–89(5%). Colonoscopy to the cecum was accomplished in 98%. Adenoma detection rate was 513/1810 (28%) in males and 358/2158 (17%) in females. Colon cancer was found in 19 (11 M, 8 F). 8(42%) of cancers were T1, 5 (26%) T2 and 6 (32%) T3. From 2004 to 2006, 229 colorectal cancers were reported to our tumor registry. The T stages were T1 (25%), T2(24%), T3(27%) and T4(24%). Complications included perforation in 2 (0.05%). One perforation was instrumental and one was post polypectomy. Post polypectomy bleeding occurred in 6 (0.15%). There was no mortality.

**Conclusion:** Average risk screening colonoscopy is safe and finds significant numbers of adenomas and early cancers when done in the community hospital setting. Males are under represented in the total screened population but over represented in both polyp and cancer detection. Efforts need to be taken to encourage participation in colon cancer screening especially among the male population.

1195

### Body Mass Index, Waist-to-Hip Ratio, Family History and Risk of Colorectal Cancer. A Prospective Study

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**Purpose:** To examine the association of body mass index BMI, waist-to-hip ratio WHR and family history FH with the incidence of colon adenoma and colorectal carcinoma CRC in Brazilian adults.

**Methods:** From January 2006 to December 2006, consecutive patients  $\geq 50$  years referred to colonoscopy were subject to measurement of BMI, WRH and FH for CRC. Exclusion criteria: Inflammatory bowel disease, Lynch syndrome, familial polyposis of the colon, chronic liver disease and chronic renal failure. For anthropometric data, gender was analysed separately. Chi square was used to compare proportional data whereas the student's t test was used to compare means.  $P < 0.05$  was considered significant

**Results:** 489 patients were enrolled in this study, being 171 men and 318 women. Man with tumor (CRC and adenoma) n 80, age  $64 \pm 9.5$ , BMI  $26 \pm 4$  and WHR  $0.95 \pm 0.05$ ; woman with tumor (CRC and adenoma) n 137, age  $65 \pm 9.9$ , BMI  $27 \pm 4.8$  and WHR  $0.89 \pm 0.08$ ; man without tumor n 91, age  $64.6 \pm 10$ , BMI  $26 \pm 3.7$  and WHR  $0.92 \pm 0.21$ ; woman without tumor n 181, age  $64 \pm 9$ , BMI  $26.3 \pm 4.7$  and WHR  $0.89 \pm 0.07$   $P > 0.05$ . FH was positive for 76 (28%) patients without tumor and for 73 (36.6%) with tumor  $P < 0.05$ . Adenoma was found in 50 (29%) of men and 73 (23%) of women

**Conclusion:** Our data suggest a relationship of CRC with a FH, but not with BMI and WHR ratio. This is an ongoing study. We have no disclosure to make.

1196

### Ethnic Differences in Findings on Screening Colonoscopy

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**Purpose:** There is increased incidence and mortality from colon cancer (CCA) in African Americans, and CCA screening in this population is underutilized. Some have suggested earlier screening in African Americans. However, there is little data on the findings of screening colonoscopy in this population. We performed a retrospective analysis to compare findings of polyps/CCA in African Americans to Caucasians undergoing screening colonoscopy at our institution.

**Methods:** We collected data for colonoscopies performed at our institution in 2004 and identified all screening/surveillance colonoscopies (N = 587). We assembled 2 cohorts: all patients (pts) who were self-identified as African-American or Black (N = 78) and all pts who were self-identified as Caucasian or White (N = 502). We collected data for age, colonoscopy findings including number and location of polyps and presence of advanced lesions (adenoma >1 cm, tubulovillous histology and CCA). Proportions were compared by chi-square analysis; means were compared by t-test. All significant P values reported for  $P < .05$ .

**Results:** There was no significant difference between the 2 groups for age, previous endoscopy, h/o polyps, h/o CCA, and family history of CCA. We

	Results		
	% of White pts	% of Black pts	P
Polyps	40.8	38.5	NS
Adv Polyps	12.4	19.2	.096
CCA	2.2	3.8	NS
Prox Polyps	18.3	26.9	.075
Prox Adv Polyps	5.4	14.1	<.01
Prox CCA	1.2	3.8	.078
Distal Polyps	30.5	17.9	<.05
Distal Adv Polyps	9.0	5.1	NS
Distal CCA	1.0	0.0	NS

found there was no difference in% pts with any findings of polyps or CCA. There were significantly fewer black pts with any distal polyps (17.9 vs 30.5%,  $P < .05$ ) and significantly more black pts with proximal advanced polyps (14.1 vs 5.4%,  $P < .01$ ). There was a trend for more black pts with findings of any advanced polyps (19.2 vs 12.4%,  $P = .096$ ), proximal polyps (26.9 vs 18.3%,  $P = .075$ ), and proximal CCAs (3.8 vs 1.2%,  $P = .078$ ). There was no difference between the 2 groups for having distal advanced polyps, distal CCAs, multiple polyps, or multiple advanced polyps.

**Conclusion:** In our analysis, we found that there were significantly more black pts with proximal advanced polyps. There was also a trend for more black pts with findings of advanced polyps, proximal polyps and proximal CCAs. Flex sigmoidoscopy may be inadequate for CCA screening in this population, and African Americans should undergo colonoscopy with particular attention for proximal lesions. However, further larger prospective studies are needed.

## 1197

### Reasons for Delay in the Diagnosis of Colon Cancer under Colonoscopic Watch – Pilot Study

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**Purpose:** Two questions are important to evaluate the quality of colonoscopic screening of cancer. How often colon cancer is not detected at the first examination? How often is it diagnosed on follow up? Our aim is to address this issue by a retrospective data analysis.

**Methods:** Review of our pathology department's database identified 300 consecutive cases of invasive colon cancer (2002–06). Then, the endoscopy database was analyzed to check whether the colon cancer was diagnosed at the first colonoscopy or diagnosed during follow up. Demographic data, cancer characteristics, colonoscopy and histology findings and outcome on follow up were collected. Analysis was done to identify factors for the delay in diagnosis as shown in the table. Patients with poor preparation or patients in whom cecum could not be reached were grouped as unsatisfactory exam.

**Results:** 264 colon cancers were diagnosed at the first colonoscopy and 36 cases not identified at the first colonoscopy were diagnosed during FU.

**a. Delay in the diagnosis of cancer:** The median interval between colonoscopic diagnosis of cancer and previous colonoscopy unremarkable for cancer was 418.5 days (11–3137 days); 278 days (14–2854 days) in those with an unsatisfactory colonoscopy and 632 days (11–3137 days) in those with a satisfactory examination.

Colon cancer was diagnosed in 3 months in 12 patients, 3 to 60 months in 21 patients and after 60 months in 3 patients after a previous colonoscopy unremarkable for cancer.

**b. Reasons for the delay in diagnosis** (see table):

**c. Demographics and Characteristics:** Mean age: 69 yrs (M:F:1:1); Indications for repeat colonoscopy: occult/overt GI bleeding: 16; previous polyps: 9; abnormal imaging: 3; others: 8. Cancer location: Right colon: 29 patients; Left colon: 7. Cancer staging (N = 31): I: 15; II: 7; III: 3 and IV: 6. All but 2 patients are surviving.

**Conclusion:** Although colon cancer is diagnosed at the first colonoscopic examination in most patients, in 10% of patients the diagnosis was not obvious at first examination. Reasons for the delay in diagnosis include failure to repeat the exam after unsatisfactory exam, failure to identify the lesion as cancer or rapidly growing tumor.

## 1198

### Adherence to Polyp Surveillance Guidelines at an Academic VA Medical Center

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**Purpose:** Recent surveys suggest that physicians recommend repeat colonoscopy at shorter intervals than guidelines recommend. VA physician adherence to colonoscopy guidelines is unknown. Our aim was to compare recommendations for repeat colonoscopy made by gastroenterologists at a single VA medical center to the 2006 published guidelines.

**Methods:** We collected data from 100 consecutive colonoscopies performed in February 2007. Variables included patient demographics, prior colonoscopy results, polyp characteristics, bowel prep quality, cecal intubation, polypectomy completeness, and recommendations for repeat colonoscopy.

**Results:** Seven patients with inflammatory bowel disease were excluded from further analysis. The remaining sample was 95% men, 53% Caucasian, 43% African-American, 5% < 50 years, 41% 50–59 years, 28% 60–69 years, 17% 70–79 years, 9% ≥ 80 years. The colonoscopy was the first for 41%. Findings were: cancer (2), multiple adenomas (35), 1–2 adenomas < 10 mm (15), hyperplastic polyps only (25), no polyps (16). For 74 of 93 (80%), the physician recommendation followed the guidelines for a given endoscopic and histologic finding and, where applicable, for prior history of neoplasia. In addition, the following patients were recommended for earlier follow-up, but had documented explanations: 2 patients with no polyps had poor prep; 1 patient with hyperplastic polyps had an incomplete colonoscopy; 4 patients with multiple adenomas had > 10 polyps each; and 4 other patients with multiple adenomas had incomplete polypectomy. The remaining patients, 8/93, were recommended for earlier follow-up without documentation of mitigating circumstances.

In summary, considering not only the guidelines for polyp characteristics and prior neoplasia, but the guideline comments regarding poor bowel preparations, complete colonoscopy, greater than 10 adenomas, and incomplete polyp removal, 85/93 or 91% of the recommendations followed guidelines.

**Conclusion:** Unlike other settings, there was no evidence of significant overuse (or underuse) of colonoscopy at this VA facility. The 99% rate of cecal intubation is on par with quality guidelines. The incidence of poor bowel preparation (2%) and incomplete polypectomy (4%) were low, but should be considered for further quality improvement. Examination of a national sample of VA facilities is warranted, but this study suggests that VA gastroenterologists adhere to guidelines for repeat colonoscopy leading to appropriate allocation of this resource.

## 1199

### Open Access Colonoscopy: An Acceptable Strategy To Boost Colon Cancer Screening Rates

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Colonoscopy Reasons for delay in diagnosis	Unsatisfactory Cancer not seen: unsatisfactory colonoscopy	Satisfactory			
		Cancer not seen: normal colonoscopy	Cancer not seen: incidental polyps	Cancer seen: suspected to be cancer	Cancer seen: not suspected to be cancer
No.	10	5	12	7	2
Diagnosis delay*	278	1371	848	35	74

\*Median interval (days) between cancer diagnosis and previous colonoscopy

**Purpose:** Colorectal cancer is the second leading cause of cancer related death in the United States. A conservative estimate of the demand for screening colonoscopies is at least 2.6 million per year. One attempt to improve colon cancer screening rates is open access colonoscopy (OAC), where primary care physicians can directly refer patients for colonoscopy, providing gastroenterologists with more time to perform endoscopies. Prior research on OAC has addressed the appropriateness of referrals and diagnostic yield. Little information is available regarding whether OAC is associated with shorter time waited, improved patient satisfaction, or which type of patients would benefit most from this modality. The goal of this study was to determine whether OAC is associated with a similar time to colonoscopy and similar patient satisfaction when compared to consultation-initiated colonoscopy.

**Methods:** Surveys were given to 217 patients prior to colonoscopy. In addition to demographic information, the following information was obtained: reason for colonoscopy, time waited for colonoscopy, symptoms, and a series of questions addressing patient satisfaction rated on a 1–10 scale. Patients were classified into either OAC or consultation-initiated groups, and time waited for colonoscopy and overall patient satisfaction were compared.

**Results:** Median time waited for colonoscopy for the OAC group was 8 weeks (mean 8.8, SD 10) versus 5 weeks (mean 9.4, SD 10) for the consultation initiated group (chi-square = 0.03 on one degree of freedom,  $P = 0.86$ ). Median overall satisfaction was 9 (mean 8.3, SD 2.1) in the OAC group and 9.5 (mean 8.5, SD 2.3) in the consultation group ( $P = 0.37$ ). Median time waited for colonoscopy for patients with symptoms (open access and consultation initiated combined) was 4 weeks (mean 8.3, SD 10.1) versus 8 weeks (mean 9.4, SD 10.5) for those undergoing screening colonoscopy ( $P = 0.05$ ).

**Conclusion:** Our data suggests that the time waited for colonoscopy and patient satisfaction is similar between open access and consultation-initiated colonoscopy. We conclude that OAC is a viable alternative to consultation-initiated colonoscopy with respect to time to endoscopy and overall patient satisfaction, a fact that is increasingly important when manpower in the field is critically low.

## 1200

### Screening Colonoscopy in Patients Older Than 80 Years

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**Purpose:** Screening colonoscopy for age 80+ is controversial, given age-associated comorbidities, surgical candidacy, and life expectancy. We performed a retrospective review to determine the yield of screening/surveillance colonoscopies in this age group and compared findings on colonoscopy to those in patients (pts) <80 yo.

**Methods:** We collected data for all screening/surveillance colonoscopies performed at our institution in 2004 ( $N = 587$ ). We assembled 2 cohorts: pts who were  $\geq 80$  yo ( $N = 56$ ) and pts who were <80 yo ( $N = 531$ ) at time of procedure. We collected data for colonoscopy findings including number and location of adenomas, histology, presence of advanced adenomas (size >1 cm, villous features, high grade dysplasia), and colon cancer (CCA). Survival for >2.5 yrs from time of procedure for patients  $\geq 80$  yo was also recorded. Proportions were compared by chi-square; all significant  $P$  values reported for  $P < .05$ .

**Results:** Colonoscopies for pts  $\geq 80$  yo represented 9.5% of procedures. There was no significant difference between the 2 groups for previous endoscopy or h/o CCA; however, more pts <80 yo had a (+) family h/o CCA (18.6 vs 5.4%,  $P < .05$ ). There was no difference in percentage of pts between the 2 groups for advanced adenomas or cancer. Significantly more pts  $\geq 80$  yo had adenomas (35.7 vs 20.4%,  $P < .01$ ). There were significantly more pts  $\geq 80$  yo with proximal adenomas (19.6 vs 9.8%,  $P < .05$ ). There was a trend for more proximal advanced adenomas (12.5 vs 6.0%,  $P = .06$ ) in pts  $\geq 80$  yo. There was no difference between the 2 groups for proximal CCAs, distal advanced adenomas, or distal CCAs. 39 pts  $\geq 80$  yo (72.2%) were alive >2.5 yrs after procedure. When compared to percentage of pts

70–79 yo who were alive >2.5 yrs after colonoscopy, there was no significant difference between the 2 groups (72.2% vs 82.2%,  $P = \text{NS}$ ).

**Conclusion:** Screening colonoscopy is controversial in pts  $\geq 80$  yo. In our study more pts  $\geq 80$  yo had adenomas. There was a trend for more pts  $\geq 80$  yo with proximal advanced adenomas. After 2.5 yr follow-up, 72.2% pts  $\geq 80$  yo were alive. This suggests that pts  $\geq 80$  yo may still benefit from screening colonoscopy; however, additional studies are needed.

	Results		
	% of Pts <80 yo	% of Pts $\geq 80$	$P$
Adenoma	20.4	35.7	<.01
Adv Adenoma	13.2	16.1	NS
CCA	2.1	5.4	NS
Prox Adv Adenoma	6.0	12.5	.06
Survival >2.5 yr	82.2 (70–79 yo)	72.2	NS

## 1201

### Distribution of Colon Neoplasia in Chinese Patients: Implications for Endoscopic Screening Strategies

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**Purpose:** Our aim was to measure the prevalence and distribution of colonic neoplasia in Chinese adults, and to estimate the sensitivity of sigmoidoscopic screening strategies for detecting those with advanced neoplasia.

**Methods:** Asymptomatic, average-risk Chinese adults aged  $\geq 50$  years underwent screening colonoscopy. The prevalence and distribution of colonic neoplasia and advanced neoplasia (defined as an adenoma  $\geq 10$  mm or with villous, high-grade dysplastic or malignant features) were recorded and the outcomes of various sigmoidoscopic screening strategies estimated.

**Results:** Of 1382 subjects (833 men, 549 women; mean age 58.8 years) included, 243 (18%) had colorectal neoplasia and 72 (5.2%) had advanced neoplasia. Neoplasia prevalence was significantly higher in male and older patients. There were no significant differences in neoplasia or advanced neoplasia distribution between men and women. Overall, 24 patients had advanced neoplasia in the proximal colon, of whom 4 had synchronous distal neoplasia. The estimated sensitivity for detecting patients with advanced neoplasia was 72% if we assumed screening sigmoidoscopy was performed, with follow-up colonoscopy for those with distal neoplasia; 165 patients would need to undergo colonoscopy. If instead we assumed follow-up colonoscopy was done only for patients with distal advanced neoplasia, the estimated sensitivity would decrease slightly to 71% but the number of colonoscopies would decrease substantially to 51. The estimated sensitivity of screening sigmoidoscopy (with follow-up colonoscopy for patients with distal neoplasia) was not statistically different in men and women (75.5% versus 63.2%;  $P = 0.3$ ). If we assumed that colonoscopy was performed only for patients with distal advanced neoplasia, there was also no significant difference between men and women (73.6% versus 63.2%;  $P = 0.39$ ).

**Conclusion:** In average-risk Chinese adults, screening sigmoidoscopy is estimated to detect more than two-thirds of patients with advanced neoplasia. In societies with limited health care resources, performing colonoscopy only on Chinese patients with distal advanced neoplasia is a screening approach that optimizes the return rate on colonoscopic capacity.

## 1202

### Role of Resistant Starch in Colorectal Cancer Prevention: A Prospective Randomised Controlled Trial

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**Purpose:** Colorectal cancer (CRC) is the second most common cause of cancer related death in the western world. Resistant starch (RS), defined as starch that resists digestion in the small intestine of a healthy individual, gets converted to butyrate following bacterial fermentation in the colon. Butyrate is shown to have potent anti-neoplastic effects on colon cancer cells *in vitro*. This study investigated the anti-neoplastic effects of RS in patients with CRC and its potential role of as a chemo-preventive agent.

**Methods:** A total of 65 (36 male) sporadic CRC patients were randomised to treatment (40 gm/ day) with RS or ordinary starch (OS) for 2–4 weeks. Pre-treatment and post-treatment biopsies were obtained from tumour and normal mucosa and the effects of the intervention on cell proliferation and expression of cell cycle regulatory genes *CDK4* and *GADD45A* (using real time RT-PCR) were investigated.

**Results:** The proportion of mitotic cells in the top half of the crypt (which is a valid pre-malignant marker used to assess response to chemo-preventive trials) was markedly reduced following RS treatment as compared with OS treatment ( $P = 0.028$ ) (Fig. 1). There was no effect of RS treatment on crypt dimensions or tumour proliferation index.

The expression of key cell cycle regulatory gene *CDK4* was upregulated ( $P < 0.01$ ) while that of *GADD45A* was down regulated ( $P < 0.001$ ) in the tumour tissue compared with normal flat mucosa. RS treatment for up to 4 weeks in CRC patients tended to increase *CDK4* expression ( $P = 0.07$ ) in tumour tissue. Expression of *GADD45A*, which was suppressed in cancer, was significantly upregulated ( $P = 0.048$ ) following RS treatment (Fig. 2).

**Conclusion:** RS modulates the colonic crypt cell kinetics and has potential as a chemo-preventive agent against CRC. The differential expression of key cell cycle regulatory genes may play a role in these cellular effects of RS.[figure1]

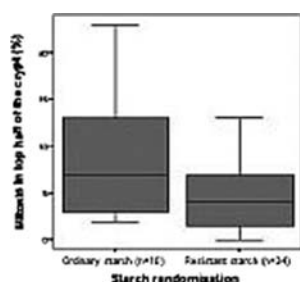


Figure 1: Mitoses in the top half of the colonic crypt following starch treatment. The middle line represents the median, the edges of the boxes represent the 25th and 75th percentiles and the whiskers represent the minimum and maximum values.

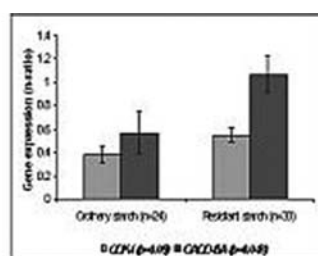


Figure 2: Expression of *CDK4* and *GADD45A* in tumours following starch treatment. The values on the Y-axis are the normalised values of expression of each gene compared with expression of the housekeeping gene *18S* and the numbers on the X-axis are the number of patients in each treatment group. (Error bars) correspond to the standard error of the mean.

## 1203

### Colorectal Cancer Screening in HIV-Infected Patients: Are They Still Being Ignored?

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**Purpose:** Although many HIV-infected patients are living well beyond 50 yr of age, there are no published data on colorectal cancer (CRC) screening in this population. Studies published in last few years suggest that although the incidence and proportion of polyps and clinically significant colonoscopic lesions are similar in normal and HIV patients, HIV patients are less likely

to undergo screening colonoscopy. The aim of this study was to determine and compare the incidence of colonoscopic screening in HIV and normal patients.

**Methods:** This study is a retrospective review of all lower endoscopies performed in the 12 month period from November 1, 2005 to October 31, 2006 at a large community hospital located in the Bedford Stuyvesant-Crown Heights area of Brooklyn, NY. The neighborhood is primarily African-American with a 1.86% prevalence of HIV in adults (the highest in NYC).

**Results:** The charts of all patients (573) who had colonoscopy during the 12 month period were reviewed. 21 of the patients were HIV-infected. Of the 316 patients who were screened for CRC, 12 (3.8%) were HIV-infected. Hence, the percentage of HIV patients screened for CRC (3.8%) was even greater than the 1.86% prevalence of HIV in the adult neighborhood population. The proportion of screening to diagnostic testing in HIV patients was comparable that in non-HIV patients (57% and 43% vs. 55% and 45% respectively). The mean age at CRC screening was about 5 years younger in HIV vs. non-HIV patients (56.5 vs. 60.8 years respectively). The bowel preparation and cecal intubation rates were adequate in screened HIV patients (92% and 100% respectively). All CRC screening was done by colonoscopy.

**Conclusion:** We found that HIV patients are being screened for CRC at a rate comparable to non-HIV patients. This may be explained by the better health care opportunities available to HIV patients in the US as well as proper referral from primary care physicians who better understand the increased life expectancy and implications for long term care including screening colonoscopy in such patients.

## 1204

### Access to Colonoscopy for Positive FOBT or Blood Per Rectum: Gender Effect at a Veteran's Hospital

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**Purpose:** Due to the relatively small percentage of women who seek medical care in the US VA medical system, it has been purported that disparities in health care delivered to women may exist in this network. While investigators have analyzed the effect of gender on colorectal cancer (CRC) screening, no study has been performed examining how accessible diagnostic colonoscopy (c-s) is once a positive FOBT (the major mode of CRC screening in the VA system) or other risk factors have been reported. Here, we present data to suggest that a gender effect exists in access to c-s.

**Methods:** From 2000–2006, patients at the Detroit VAMC were enrolled in a prospective longitudinal study examining c-s findings after stool testing. Inclusion criteria for this secondary analysis were: patients under the age of 65, having an indication other than screening for c-s (i.e., +FOBT, history of polyps, blood per rectum, anemia, change in bowel habits, newly identified family history of CRC) and inclusion of all data at analysis. Data were prospectively collected to include the indication for c-s; length of time from indication to performance of c-s; outcome of barium enema or flexible sigmoidoscopy, if applicable; age; race; and pathological findings after c-s. Students t-test,  $\chi^2$  and Fisher's exact tests were performed.

**Results:** 104 patients were included (14 females, 86 males). There were no differences seen in age, race or resultant pathology. However, among patients with any indication for colonoscopy, the time from identification of indication to diagnostic c-s was 109.5 d in females v. 228.6 d in males ( $P < 0.005$ ). When time to c-s was examined among those with new blood per rectum or +FOBT, the discrepancy was even greater (110.9 v. 236.2 d;  $P < 0.0005$ ). Patients with +FOBT or complaints of BPR tended to have pathology on c-s, though this difference did not reach significance.

**Conclusion:** This is the first study addressing access to c-s after an indication is identified. We show that females obtained c-s more expeditiously than males once an indication is established. The reasons for such a gender effect

are unclear, though recent changes in the VA system emphasizing gender-specific healthcare in the form of women's health clinics may play a role. Further studies confirming these results as well as analyzing the etiologies of this effect are warranted.

## 1205

### Physician Workforce, Socioeconomic Factors, and Colorectal Cancer Outcomes

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**Purpose:** To determine the relationship among the physician workforce, socioeconomic factors, and colorectal cancer (CRC) in Georgia.

**Methods:** Data were obtained from publicly available sources: Georgia Board for Physician Workforce, Health Resources Services Administration, U.S. Census Bureau, and Georgia Division of Public Health Online Analytical Statistical Information System (OASIS). All data were reduced to the county level and are expressed as rates per 100,000. All data were from 2004, except census data, which was from 2000. Statistical analyses were performed using SAS 9.1. Since CRC mortality rate was skewed, a log transformation was used. Pearson's correlation coefficients were used to determine associations between the predictor variables pertaining to socioeconomic status, Medicare coverage, physician workforce, and CRC outcomes. Linear regression analysis was used to model the relationship between CRC outcomes and predictor variables.

**Results:** Only 150 (94%) counties were used due to missing values. Rates of CRC hospital discharges and mortality were  $43.0 \pm 20.7$  and  $19.7 \pm 12.8$  per 100,000, respectively. The rate of primary care physicians defined as family physicians, internists, and obstetricians and gynecologists was 72.8 per 100,000 while the rate of specialty physicians defined as gastroenterologists, general surgeons, and colorectal surgeons was 7.1 per 100,000. Less than high school education ( $r = 0.44$   $P < .01$ ), MUA score ( $r = -0.19$   $P = .01$ ), median household income ( $r = -0.34$   $P < .01$ ), Medicare coverage ( $r = 0.41$   $P < .01$ ), rates of family physicians ( $r = 0.17$   $P = 0.03$ ) and gastroenterologists ( $r = -0.20$   $P = 0.01$ ) were significantly correlated with CRC mortality rates. In a linear regression model, less than high school education (adjusted  $R^2 = 18\%$ ), median household income (adjusted  $R^2 = 17\%$ ), and Medicare coverage (adjusted  $R^2 = 11\%$ ) contributed most to the variance. Workforce variables contributed less to the variance in this model: MUA score (adjusted  $R^2 = 3\%$ ), gastroenterologist rate (adjusted  $R^2 = 3\%$ ), and family physician rate (adjusted  $R^2 = 2\%$ ).

**Conclusion:** Socioeconomic factors are highly correlated with CRC mortality, and any large-scale intervention to increase CRC screening should take these into account. In addition, our data indicate that the rate of gastroenterologists has a positive impact on CRC mortality, the rate of family physicians has a negative impact on CRC mortality, and the rate of other specialties does not significantly affect CRC mortality.

## 1206

### Screening Colonoscopy in the Elderly, Is It Worthwhile?

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**Purpose:** Colorectal cancer is the third most common cause of cancer in both men and women. Mortality from CRC is related to stage at diagnosis. This study was designed to determine if screening colonoscopy leads to earlier stage of CRC diagnosis in elderly patients and, thus, improves survival. We tested the null hypothesis that patient's age  $\geq$  than 75 years of age who undergo screening colonoscopy do not have an earlier stage of disease at the time of diagnosis.

**Methods:** Patient records were obtained from the Scripps Green Hospital Cancer Registry. Our database of all patients diagnosed with pathology-proven colorectal cancer between 1/2000 and 12/2005 were queried for 1) verification of CRC, TNM stage, and location within the colon; 2) patient's age; 3) sex; and 3) presenting symptoms. Patients were excluded if they had a history of inflammatory bowel disease or familial polyposis syndrome. Patients were divided into two groups based on symptoms and by age and stage of disease at diagnosis. The stages of disease were separated at a critical point: between early (Stage 0-IIB) and late (Stage III-IV). We evaluated survival from the time of diagnosis in all patients.

**Results:** We studied 356 patients; 243 symptomatic and 113 asymptomatic. Seventeen were stage 0, 101 stage I, 99 stage IIa, 6 stage IIb, 17 stage IIIa, 55 stage IIIb, and 61 patients were stage IV. There was a sustained difference in stage of disease favoring patients who were asymptomatic versus symptomatic for the study group and for all ages between 50 and 84 years. These differences are highly significant ( $P < .00013$ ). With 100% 2-year minimum follow-up, we found asymptomatic patients had significantly improved survival when compared to symptomatic patients ( $P < .001$ ). These data disprove the null hypothesis.

**Conclusion:** Our study demonstrates significantly favorable differences in screening colonoscopies for asymptomatic vs. symptomatic patients by finding early stage colon cancer through age 84 and by improving survival. We conclude that there is a role for screening colonoscopy in asymptomatic individuals without significant comorbidities up to age 84. This is one of the first studies demonstrating that screening colonoscopy improves survival in elderly patients.

## 1207

### Effect of Initial Polypectomy Versus Surveillance Polypectomy on Colorectal Cancer Mortality Reduction: Micro-Simulation Modeling of the National Polyp Study

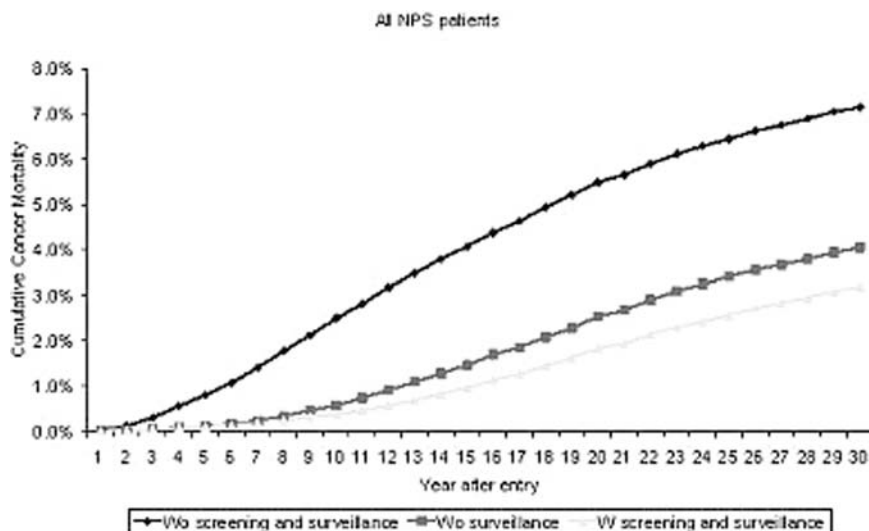
Ann G. Zauber, PhD\*, Sidney J. Winawer, MD, Iris Lansdorp-Vogelaar, MS, Marjolein van Ballegooijen, MD, PhD, Michael J. O'Brien, MD. Epidemiology and Biostatistics, Memorial Sloan-Kettering Cancer Center, New York, NY; Gastroenterology and Nutrition Service, Memorial Sloan-Kettering Cancer Center, New York, NY; Erasmus MC, University Medical Center Rotterdam, Rotterdam, Netherlands and Boston University, Boston, MA.

**Purpose:** Colorectal polypectomy with surveillance reduced colorectal cancer (CRC) incidence by 76–90% (Winawer, 1993) and colorectal cancer mortality by 69% to 92% (Zauber, DDW 2007) with 20 years of follow-up in the National Polyp Study (NPS). The relative effect of the initial polypectomy versus the surveillance colonoscopy on mortality reduction has implications for follow-up intervals, screening colonoscopy studies, and understanding the adenoma-carcinoma progression.

**Methods:** A Micro-Simulation Screening Analysis (MISCAN) model, developed at ErasmusMC Rotterdam in conjunction with the National Cancer Institute, used the NPS data to predict CRC mortality: 1) with no initial polypectomy or surveillance colonoscopy; 2) with initial polypectomy only; and 3) with both initial polypectomy and surveillance colonoscopy. The model predicted CRC mortality for up to thirty years after initial polypectomy.

**Results:** The model demonstrated a dramatic reduction in expected CRC mortality with initial polypectomy with or without surveillance and suggests that the initial polypectomy accounts for the major component of the mortality reduction (see Figure). The model predicts a modest benefit from surveillance after 10 years.

**Conclusion:** The major effect on colorectal cancer mortality reduction produced by the initial polypectomy rather than surveillance colonoscopies is consistent with the low incidence of advanced adenomas ( $\geq 1$  cm, villous component, high grade dysplasia, or invasive CRC) observed during NPS follow-up. This supports the recommendation for lengthening the surveillance intervals to 6 or more years for most patients post-polypectomy.[figure1]



1208

### Mismatch Repair Gene Mutations in Iranian HNPCC Families

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**Purpose:** Determining the MMR gene mutation carriers in HNPCC families to prevent advanced disease by early diagnosis through recommended screening tests, decreasing both mortality and morbidity rates.

**Methods:** 592 unselected colorectal cancer patients were screened for MMR mutations by immunohistochemical analysis. For patients with defects in expression of at least one of the MMR proteins, full mutational analysis was performed by PCR amplification of each exon of the respective gene, including the flanking intronic regions, followed by bidirectional sequencing. Any variation in DNA sequence was confirmed on an independent PCR prod-

uct. Paired tumoral and genomic DNA samples were used for microsatellite instability testing.

**Results:** 56/592 families fulfilled the Amsterdam Criteria II. 47/592 patients had lack of expression of MMR protein(s); 17(36%) MLH1, 25(53%) MSH2 and 5(11%) PMS2. Among them, we have found 20 mutations in 18/47 families so far. 7 mutations were novel mutations and were reported to the GenBank (GenBank accession numbers: EF570785-EF570789, EF583852 and EF125076). Genetic tests were offered to at risk family members of these patients.

**Conclusion:** Our results provide further insight into the mutational spectrum of MMR genes in Iranian HNPCC families.

1209

### Role of Tumor Necrosis Factor Gene Polymorphism (-308 and -238) in Colorectal Cancer Susceptibility

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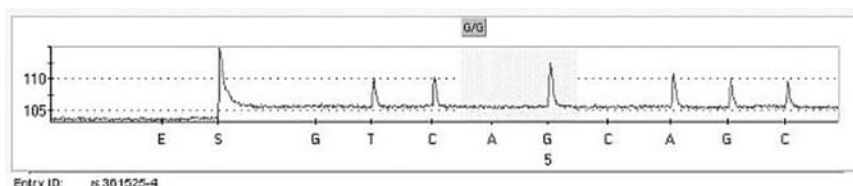
**Purpose:** The purpose of this study is to investigate the potential association of tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) promoter polymorphisms (-308 G>A and -238 G>A) with colorectal cancer susceptibility.

**Methods:** The study included 77 patients with colorectal cancer and 100 healthy controls. The polymorphisms were genotyped for these TNF- $\alpha$  polymorphisms by PCR-Pyrosequencing (Fig. 1). The distributions of TNF- $\alpha$  promoter polymorphisms were compared between cancer patients and healthy controls by the chi-square test. Odds ratios (OR) and 95% confidence intervals (CI) were also calculated.

**Results:** The Genotype distributions and allele frequencies of the -308 (rs361525) and -238 (rs1800629) TNF- $\alpha$  polymorphism in cancer patients and controls are shown in Table 1. Although the TNF-308A allele frequency was lower in the cancer group compared with the control group (7.8% vs. 14.5%) and TNF-238A allele frequency was higher (7.8% in cancer group vs. 6% in controls), the observed differences were not statistically significant ( $P > 0.05$ ). The odds ratio for cancer in subjects with the TNF-308A allele

Clinical characteristics of 56 cases with colorectal cancer who met the Amsterdam II Criteria

Characteristics		Number (Frequency)
Age at diagnosis	>50 y	35 (62.5%)
Age at diagnosis	<50 y	21(37.5%)
Sex	Male	33 (59%)
Sex	Female	23 (41%)
Location of Tumor	Left sided	37 (66%)
Location of Tumor	Proximal	19 (34%)
Tumor Stage	I	2 (3.5%)
Tumor Stage	II	21 (37.5%)
Tumor Stage	III	15 (27%)
Tumor Stage	IV	11 (19.5%)
Tumor Stage	Unknown	7 (12.5%)



**Table 1.** Distributions of the two tumor necrosis factor (TNF) polymorphisms in colorectal cancer patients and healthy controls

Polymorphism	Control/Case	Genotype Distribution				Allele Frequency	
		G/G*	G/A*	A/A*	OR(95% CI)	G*	A*
-308	Control (N = 100)	77 (77)	17 (17)	6 (6)	1.00	171 (85.5)	29 (14.5)
-308	CRC† (N = 77)	66 (13)	10 (13)	1 (1.3)	0.55 (0.24–1.25)	142 (92.2)	12 (7.8)
-238	Control (N = 100)	90 (90)	8 (8)	2 (2)	1.00	188 (94)	12 (6)
-238	CRC† (N = 77)	69 (89.6)	4 (5.2)	4 (5.2)	1.05 (0.37–3.00)	142 (92.2)	12 (7.8)

† CRC, Colorectal cancer; \* Figures in parentheses represent percentage values.

was 0.55(95% CI, 0.24–1.25) and with the TNF-238A allele was 1.05 (95% CI, 0.37–3.0).

**Conclusion:** We found no association between the -308G>A polymorphism and the -238G>A polymorphism in the promoter region of TNF- $\alpha$  and susceptibility to colorectal cancer in an Iranian population.[figure1]

## 1210

### Using Colon Cancer Screening To Aid in Identifying Obesity

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**Purpose:** While colon cancer screening aids in decreasing mortality and morbidity, other health risks may be identified during these visits. This study evaluated whether colon cancer consultations can be used to assess other health risks in African American and Caucasian women such as obesity and mammography adherence.

**Methods:** A retrospective chart review of 93 (61 African American and 33 Caucasian) female patients referred for colon cancer screening consultations over a 2 month period were performed to assess the presence of screening mammographies. Eighty-three (52 African American and 31 Caucasian) charts recorded body mass indices, which were used to assess the presence of obesity. A database was created using Microsoft Excel. Statistical analysis was performed using Fisher's exact test with significance set at  $P < 0.05$ .

**Results:** Fifty-four of 61 (88%) African American females and 28 of the 33 (85%) Caucasian females that had screening colonoscopies had undergone screening mammographies. There was no statistical significance between the two groups ( $P = 0.7477$ ). Sixty-one of the 83 patients (73%) were overweight or obese. Specifically, forty-one of 83 patients (49%) were obese and 20 of the 83 patients were overweight. There was a significant ( $P = .0002$ ) increase of obese and overweight African-Americans (88%) than caucasians (48%).

**Conclusion:** Colonoscopy screening consultations provides another opportunity to identify and counsel patients with obesity.

## 1211

### Feasibility and Results of a Colorectal Cancer Screening Program Targeting Uninsured Patients

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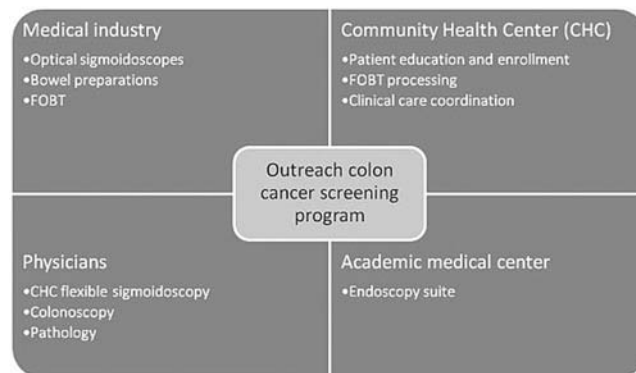
**Purpose:** Compliance with recommendations for colorectal cancer (CRC) screening remains suboptimal. Primary prevention of CRC in uninsured patients is especially problematic. We report our experience in the implementation of a CRC screening program within a free clinic and the results of its first 13 months in practice.

**Methods:** Community health administrators and physicians recruited support from the affiliate academic medical center and local representatives from medical industry (Fig. 1) to establish a CRC screening clinic. Records of patients enrolled in the community health center 50 years of age or older were screened for eligibility. Patients with a family history of CRC or symptoms of abdominal pain, weight loss, overt or occult gastrointestinal bleeding were referred directly for colonoscopy. Otherwise average risk patients were

provided verbal and written instruction on FOBT and optical flexible sigmoidoscopy (FS). FOBT negative patients underwent a FS at the community health center. Per current guidelines, follow-up recommendations were provided based on FS results.

**Results:** 178 patients (mean age 59.2, 56.2% female, 70.3% Hispanic, and median annual income US\$8,280) underwent FS following negative FOBT. 5.2% of patients eligible for FS refused to participate. 22 patients (12.4%) were found to have a tubular adenoma during FS and referred to colonoscopy. Of these, 1 patient was found to have adenocarcinoma in-situ and 1 patient with invasive adenocarcinoma. Patients found to have a tubular adenoma were significantly older (62.4 years compared to 58.8 years,  $P = 0.04$ ) compared to normal subjects; sex, ethnicity and median annual income was not associated.

**Conclusion:** The implementation of a colorectal cancer screening program coordinating a free clinic, an academic medical center, physicians and the medical industry is feasible and sustainable. The prevalence of adenomatous polyps among a predominantly Hispanic population is significant. Future studies should focus on the potential economic benefit of this type of primary prevention on reducing health care costs.[figure1]



## 1212

### Adherence to Screening Colonoscopy in a VA Setting

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**Purpose:** Adherence (completion) rate for screening colonoscopy is reported between 50% and 70%. Adherence is dependent on patient's scheduling and patient's compliance. The main reason for non-adherence is the lack of patient-driven scheduling. In the VA system, patient's scheduling is *GI-service-* rather than *patient-driven* with an unknown adherence rate. **Aim:** Determine the adherence rate to screening colonoscopy in a VA Hospital.

**Methods:** Three scheduling strategies were tested: the PCP generated an electronic (e-) consult to GI who contacted and scheduled the patient (Group 1); after a discussion with patient, the PCP generated an e-consult to GI AND each patient was given written information detailing CRC and screening colonoscopy and prompting them to **CALL** that day to schedule the procedure (Group 2); after a discussion with the patient, the PCP generated an e-consult to GI AND gave them a card that prompted them to **STOP BY** the GI section today and schedule the colonoscopy (Group 3). One week



Adherence rates at 1 month

Scheduling	Group 1	Group 2	Group 3	Overall
Patient-driven	0	24/72 (33.3%)a	19/34 (55.9%)a, b	43/135 (31.9%)
GI Service-driven	23/29 (79.3%)	37/72 (51.4%)a	12/34 (35.3%)a	72/135 (53.3%)
Overall	23/29 (79.3%)	61/72 (84.7%)	31/34 (91.2%)	115/135 (85.2%)

a vs Group 1; b vs. Group 2;  $P < 0.05$ ; Chi square analysis

after receipt of the e-consult, GI phoned the patients who did not initiate contact to schedule the procedure. The adherence rate was determined after 1 month.

**Results:** 184 consults were received (37, 101 and 46 in Groups 1, 2 and 3, respectively). Excluded from the analysis were 10 patients who did not call back after leaving messages 3 times, 12 who refused to undergo colonoscopy, 5 who had inappropriate referrals (surveillance, acute medical contraindications or other reasons), and 22 who were scheduled to have colonoscopy beyond 1 month. The data of 135 patients were analyzed. Table 1 shows the adherence rate for each of these 3 groups.

**Conclusion:** 1) Implementation of patient- and GI- driven scheduling strategies at this VA Hospital resulted in an overall adherence rate at 1 month of 85%, a much higher rate than that reported in community practice (50 to 70%). 2) The strategy of instructing patients to go to GI immediately resulted in the highest patient-driven (56%) and highest overall (91%) adherence rate.

## 1213

### Disparities in Colon Cancer Screening – A Population Study

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**Purpose:** The screening rates for colorectal cancer are lower in certain racial and ethnic subgroups. We analyzed colorectal screening adherence across 6 geographically distinct multiracial communities in Chicago, Ill. We evaluated various barriers to colorectal screening.

**Methods:** In 2002–2003, a comprehensive household health survey was conducted in six community areas with 1,700 households in English and Spanish. As a part of the survey, individuals over the age of 50 were asked whether they had ever had colorectal cancer screening with either an endoscopic exam or blood stool test.

**Results:** The proportion of participants over the age of 50 who reported ever having a blood stool test, or endoscopic test ranged from 42% to 70%, and 36 to 54% across the 6 communities. The community with the highest screening proportion for an endoscopic test (54%) was predominantly white with the lowest poverty level. The communities with the lowest screening proportion for an endoscopic test had the highest poverty levels and were composed of predominantly, blacks and Hispanics. Within the 6 communities, Mexicans (33%) were less likely to report screening with a blood stool test compared with whites (65%) ( $P < 0.0001$ ). They were also less likely to report ever having a sigmoidoscopy/colonoscopy. Participants whose home was primarily Spanish speaking reported a lower adherence to occult blood screening (31%), and endoscopic screening (38%) compared with homes where English was the primary language (66%) ( $P < 0.0001$ ). Having a regular primary care physician, getting medical care other than when sick, and having any doctor visits in the past 12 months were all associated with adherence with colorectal cancer screening ( $P < 0.05$ ).

**Conclusion:** Adherence to colorectal cancer screening varies widely between different communities. Community level analysis of screening adherence would assist the shaping of culturally meaningful prevention efforts.

## 1214

### Which Adenoma Characteristic Has the Strongest Effect on Predicting Advanced Neoplasia or Numerous Adenomas on Follow up Colonoscopy?

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**Purpose:** Adenoma size, number and pathology are independently associated with recurrence of advanced neoplasia (AN). The Multi-Society Task Force (MSTF) recommends different surveillance intervals based on adenoma features: 5–10 yrs for individuals with low recurrence risk [LR] ( $< 3$ ,  $< 10$  mm, TA) and 3 yrs for those with high recurrence risk [HR] ( $> 2$ ,  $\geq 10$  mm, or advanced neoplasia). Our aim was to determine the magnitude of the effect of each factor in predicting recurrent AN or being classified as HR at FU colonoscopy.

**Methods:** Data from subjects in the placebo arm of 3 postpolypectomy chemoprevention trials were used. Subjects were divided into LR or HR based on MSTF criteria. AN was defined as adenoma  $> 9$  mm or with any villous component/SD. Multivariate regression analysis was used to obtain risk ratios for baseline adenoma factors, looking first at baseline risk status (HR vs LR) and then size, histology and number of adenomas in a second model. All models included age, sex, study, and follow-up time as covariates.

**Results:** 800 subjects with a baseline adenoma(s) and who underwent complete polypectomy were included. The mean time to FU colonoscopy was 37 months. HR status at baseline was significantly associated with recurrent AN, RR 1.9 (1.2–3.0,  $P = 0.01$ ) and HR status on FU, RR 2.1 (1.5–3.1,  $P < 0.0001$ ). When individual adenoma features were studied, adenoma multiplicity was associated with both outcomes, pathology was not associated with either outcome and large size was only associated with AN (Table).

**Conclusion:** The number of adenomas ( $> 2$ ) is the strongest predictor of risk of recurrent AN and being classified as HR at FU. Colonoscopists should be diligent in efforts to detect synchronous neoplasia regardless of size in order to recommend the proper postpolypectomy interval.

Baseline Adenoma Factor	Effect of Adenoma features on Recurrence			
	Advanced Adenoma		HR status	
	*RR (95% CI)	P value	*RR (95% CI)	P value
Size (mm)				
6–9 vs $> 9$	0.98 (0.51–1.89)	0.96	1.05 (0.64–1.72)	0.85
$> 9$ vs $< 6$	1.73 (1.03–2.90)	0.04	1.47 (0.96–2.26)	0.08
Pathology				
VA vs TA	1.11 (0.67–1.85)	0.68	1.31 (0.87–1.98)	0.20
Number				
$> 2$ vs $< 3$	1.69 (1.06–2.69)	0.03	2.25 (1.55–3.27)	$< 0.001$

\*Adjusted

## 1215

### Adenomas Are Detected More Often on Morning Than Afternoon Screening Colonoscopy

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**Purpose:** Effective colonoscopy (COL) depends on adenoma detection and removal. We postulate that adenoma detection may be lower in afternoon (PM) than morning (AM) COL due to factors other than inadequate bowel

Demographic and Endoscopic Features of Subjects

Characteristic	AM	PM	P value
Mean Age	58	59	0.22
Female	54%	50%	0.012
Indication (Average risk, Personal Hx, Family Hx, Increased risk)	(53.2%, 31.7%, 10.7%, 4.5%)	(59.9%, 26.6%, 8.9%, 4.5%)	<0.001
Fellow participation	4.7%	1%	<0.001
Diverticulosis seen	32.1%	27.1%	0.001
Predictors of Adenoma Detection			
Factor		O.R. (95% CI)	P value
Time of day	AM vs PM	1.2 (1.04, 1.4)	0.008
Age	Every 5 year increase	1.1 (1.08, 1.2)	<0.0001
Gender	Male vs Female	1.6 (1.4, 1.9)	<0.0001
Indication	Personal Hx vs Ave risk	2.0 (1.7, 2.4)	<0.001
Diverticulosis	No vs yes	1.2 (1.01, 1.4)	0.036

prep or incomplete COL. Our aim was to determine the effect of timing of screening COL on adenoma detection.

**Methods:** The records of 9063 COL performed in 2006 at a tertiary care gastroenterology department were reviewed. Data including patient demographics, indication for COL, time of COL (AM versus PM), COL findings, presence of adenomas, and adenoma size, number, pathology were obtained. Patients with incomplete COL, inadequate bowel prep, prior colonic resection, inpatient status, and COL done for indication other than screening were excluded. AM COL was defined as COL that started before 12 PM and PM COL as an exam that started after 12 PM. Wilcoxon rank sum and Chi square tests were used. Multivariable logistic regression analysis was used to study factors for adenoma detection.

**Results:** 3621 COL included. 1749 (48.3%) were done in AM and 1872 (51.7%) in PM. Adenomas were detected in 29% of AM and 25% of PM COL ( $P$  0.008). More females, subjects with increased risk of neoplasia, fellow participation in exam and diverticulosis were noted in the AM group (Table 1). No difference in the size ( $P$  0.4), number ( $P$  0.8), location ( $P$  0.4), or pathology of adenomas ( $P$  0.4) was observed between AM and PM COL. In the multivariable analysis, AM COL were significantly associated with higher adenoma detection as were male gender, increased risk status and older age (Table 2).

**Conclusion:** AM colonoscopy is an independent predictor for increased adenoma detection. The reason and implications of this finding should be considered and studied further.

## 1216

### Findings on Surveillance Colonoscopy in Patients with Low-Risk Polyps on Initial Colonoscopy

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**Purpose:** Adenomatous polyps are commonly found on colonoscopy with current guidelines recommending a detection rate of 25% in men and 15% in women. Studies show that screening colonoscopy with post-polypectomy surveillance reduces colon cancer risk, but the optimal timing of surveillance exams in patients with low risk polyps is uncertain. This study describes the prevalence of adenomatous polyps on follow-up after a colonoscopy finding only 1–2 small tubular adenomas. We hypothesized that the prevalence of adenomas and advanced adenomas identified on the 3rd colonoscopy would be low and even lower if the 2nd colonoscopy had no adenomas identified.

**Methods:** We compiled a retrospective cohort of patients  $\geq 49$  yrs old who had 1–2 small ( $<10$  mm) tubular adenomas identified and removed on colonoscopy and 2 subsequent colonoscopies, each  $\geq 11$  months apart. Exclusion criteria included a history of polyps, cancer or surgery of the colon

or inflammatory bowel disease. Advanced adenoma was defined as  $\geq 1$  cm or with tubulovillous or villous histology or high-grade dysplasia.

**Results:** We identified 1002 patients who had  $\geq 3$  colonoscopies performed at an academic medical center from 1993 to 2006. 88 patients (52 men, 36 women, 66% white, 30% black, 4% other) met inclusion criteria. The median age at 1st colonoscopy was 60 (range 49–85). The median time between 1st and 2nd colonoscopy and between 2nd and 3rd colonoscopy was 33 months (range 11–78) and 37 months (range 11–102), respectively. At the 2nd and 3rd colonoscopy, 31/88 (35.2%) patients and 26/88 (29.6%) patients had at least 1 adenoma, respectively. At colonoscopy #2, 4/88 (4.6%) patients had an advanced adenoma or  $\geq 3$  adenomas. At colonoscopy #3, only 3/88 (3.4%) patients had advanced adenomas (95% CI 0.7–9.6%). One of these 3 had an advanced adenoma on the 2nd colonoscopy, and the other 2 had no adenomas on the 2nd colonoscopy. Among the 56 patients without adenomatous polyps at colonoscopy #2, the prevalence of any and advanced adenomas on colonoscopy #3 was 25% (95% CI 14.4%–38.4%) and 3.6% (95% CI 0.4%–12.3%), respectively. The presence of adenomas on the 3rd procedure was not significantly associated with whether it was performed  $<$  or  $> 3$  years from the 2nd procedure.

**Conclusion:** In patients with 1–2 small tubular adenomas on initial colonoscopy the prevalence of adenomas and advanced lesions on the third colonoscopy is high enough to justify continued surveillance -within 5 years-even if no adenomas are found on the 2nd colonoscopy.

## 1217

### Low Frequency of Colon Polyps in Association with Diverticulosis

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**Purpose:** Prior research has suggested that there is a lower frequency of colon cancer in areas of colon affected by diverticulosis. The aim of this study was to determine the prevalence of adenomatous polyps in association with adjacent diverticulosis.

**Methods:** 600 consecutive colonoscopy reports from a single endoscopist at our institution were reviewed to determine the prevalence, location, and co-association of diverticulosis and adenomatous polyps noted during colonoscopy. Cases with incomplete evaluations were excluded, leaving 589 colonoscopies for inclusion in this study.

**Results:** Of 589 colonoscopies, 308 (mean age 63) exhibited diverticulosis, while the remaining 281 (mean age 58) did not. 142 (46%) of the 308 patients with diverticulosis were found to have polyps, and 128 (46%) of the 281 patients without diverticulosis were found to have polyps. To analyze the co-association of polyps and diverticulosis in the same segment of colon in affected patients, we subdivided the data by colonic segment. Of the 308

patients with diverticulosis, 252 patients had diverticulosis in the rectosigmoid colon, 188 patients in the descending colon, and 103 patients in the proximal colon. In a subset analysis, concurrent polyps (in the same segment of colon) were found in 17/252 (7%) of patients who had diverticulosis in the rectosigmoid colon, 10/188 (5%) in the descending colon, and 18/103 (17%) in the proximal colon. Among the patients who did not have diverticulosis in those same segments of colon, polyps were found in 56/337 (17%) of patients without diverticulosis in the rectosigmoid colon, 73/401 (18%) in the descending colon, and 133/486 (27%) of patients in the proximal colon. Thus, the prevalence of adenomatous polyps in colonic segments affected by diverticulosis as opposed to the same segment unaffected by diverticulosis was 7% v. 17% for the rectosigmoid colon ( $P = 0.008$ ), 5% v. 18% for the descending colon ( $P = 0.002$ ), and 17% v. 27% for the proximal colon ( $P = 0.02$ ).

**Conclusion:** The frequency of adenomatous polyps was significantly lower in colonic segments with associated diverticulosis as compared to colonic segments without associated diverticulosis. Despite a similar frequency of polyps overall, patients were significantly less likely to have concurrent polyps in the colonic segment affected by diverticulosis (rectosigmoid, descending, and proximal colon). These data are consistent with the previous finding of a lower prevalence of colon cancer in segments of colon affected by diverticulosis.

## 1218

### The Influence of Race and Gender on Colon Polyp Incidence after Polypectomy

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**Purpose:** To determine the effect of gender and race on incidence of new polyp formation among individuals undergoing polypectomy at colonoscopy for screening or minimal symptoms. There appear to be discrepancies between the effect of African-American (AA) race and gender on the risk of colon cancer vs. the prevalence of colon polyps. One explanation is a variable growth pattern and/or recurrence rate. Our recent polyp prevalence study (DDW 2007) showed no effect by race, but males had an increased polyp prevalence.

**Methods:** GI-Trac is an endoscopy database containing colonoscopy information prospectively collected over 10 years at the Medical University of South Carolina (MUSC), including indications and symptoms, prior intervention, disease risk factors, ASA comorbidity index, procedure times, preparation quality, findings (including polyp size, location, and removal), and completeness to the cecum. Patients who had a colonoscopy for screening or minimal symptoms and came back to MUSC for another colonoscopy over the 10 years were included. A Cox proportional hazards model was built to assess the effect of gender and race corrected for selected confounders on polyp recurrence, determining adjusted hazard ratios (aHR) for "polyp-free survival". A random sample's histology reports were manually reviewed to assess for possible racial/gender differences in polyp histology.

**Results:** 760 (20%) of 3732 subjects had polyps on a colonoscopy for screening or minimal symptoms in our prevalence study, with roughly half eligible for >5 year follow-up. Cecal intubation rate was 98.6%. A random sample of pathology ( $N = 40$ ) from this cohort showed there was no significant racial difference in the proportion of polyps that were adenomatous (whites 68% vs. AA 60%,  $P = 0.60$ ). 57 subjects had a follow-up colonoscopy at MUSC a median of 3.58 years after their index procedure: 18 were male, 7 AA, 19 were over age 65 and 35 (61.4%) had a polyp recurrence. Neither gender (aHR = 0.98; 95% CI (0.43 – 2.21)) nor race (aHR 1.89; 95% CI (0.70 – 5.24)) significantly predicted recurrence of polyps.

**Conclusion:** Gender and race do not appear to predict recurrence of colon polyps after polypectomy; gender- and race- specific recommendations for surveillance colonoscopy are not supported. Larger sample sizes may be needed to further improve the precision of these estimates.

## 1219

### Exploring Fund of Knowledge, Beliefs and Attitudes about Colo-Rectal Cancer Screening. Results of a Patient Survey Undergoing Screening Colonoscopy

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**Purpose:** Patient's fund of knowledge, beliefs and attitudes towards CRC screening are varied and is not known whether these affect compliance and adherence to the different CRC screening strategies. We test the hypothesis that certain patient attributes determine their knowledge of colorectal cancer and screening.

**Methods:** Patients presenting for screening colonoscopy were asked to voluntarily and anonymously fill out a 21-question survey upon checking in to the endoscopy unit. In addition to age, race and gender, questions explored their understanding of why they had to undergo screening colonoscopy, whether they perceived their providers had given them discussions of the colonoscopy, and questions that determined their fund of knowledge about colon cancer and colorectal cancer screening.

**Results:** 151 patients completed the survey. The mean age was 62.8 years and the majority were men (5.3% were women). Significantly different knowledge scores exist between subjects who indicated they knew or did not know why they were having colonoscopy, whether their providers discussed details of colonoscopy, and if they would recommend colonoscopy to family members. Subjects who knew about unsedated colonoscopy had a significantly higher score in terms of willingness to consider use of unsedated colonoscopy (Table 1). Knowledge score was not dependent on first time screening colonoscopy, history of fecal occult blood testing, delayed screening, prior refusal of colonoscopy, and family history of colon cancer.

**Conclusion:** There is significant room for improving patient's overall and specific colonoscopy screening fund of knowledge. The effects of such improved education upon adherence and compliance need to be studied further.

Results (Mean ± SEM)	N	Knowledge Score Maximum = 15)	P (Unpaired t)
Did not know why having colonoscopy	21	6.4 ± 0.3	0.03
Knew why having colonoscopy	130	7.4 ± 0.2	
Provider did not discuss colonoscopy	95	6.9 ± 0.2	0.003
Provider did discuss colonoscopy	55	7.9 ± 0.3	
Would not recommend screening to family members	4	4.8 ± 1.4	0.004
Would recommend screening to family members	114	7.7 ± 0.2	
		Consider Unsedated Colonoscopy (0 = no; 1 = yes)	
Did not know about unsedated option	71	0.28 ± 0.05	0.024
Knew about unsedated option	45	0.49 ± 0.08	

1220

**Obesity (BMI  $\geq 30$ ) Has Highest Attributable Risk for Colorectal Neoplasia in Asymptomatic Women**

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**Purpose:** Screening for colorectal cancer is currently recommended to begin at 50 for most patients. This recommendation does not include other important factors such as BMI and smoking. Using these factors may allow for more effective screening, possibly by requiring less intense screening for some 50 year old women as suggested by one expert (Lieberman AJG 2005). Our goal was to determine population attributable risk (PAR) for age, smoking, BMI and family history in a screening population for women.

**Methods:** We collected age, gender, height, weight, family history of colorectal cancer, smoking history, meds, alcohol use and dietary history from asymptomatic patients >40 years presenting for screening colonoscopy. Patients were divided into those with BMI <30 kg/m<sup>2</sup> and  $\geq 30$  kg/m<sup>2</sup>. For smoking, patients were divided into three groups: 1) Heavy exposure- those who had smoked > 10 pack years and who were currently smoking or had quit in the past 10 years 2) Low exposure- those who had smoked <10 pack years or who had quit >10 years ago regardless of total pack years 3) No exposure- those who never smoked. Significant colorectal neoplasia was defined as large (>10 mm) adenoma, villous adenoma, multiple (>2) adenomas, high-grade dysplasia or cancer. All results were confirmed using advanced neoplasia as an endpoint.

Significant Neoplasia in Asymptomatic Women

Risk Factor	N	% exposed	Odds Ratio	PAR	P-value
Age <50	239	19.1	1.0	—	—
Age 50–59	511	40.8	1.03	1.2	—
Age 60–69	328	26.2	1.45	10.6	—
Age >69	174	13.9	2.43	16.5	0.01
BMI <30	871	69.5	1.0	—	—
BMI $\geq 30$	381	30.4	1.84	20.4	.007
— FH CRC	1031	82.3	1.0	—	—
+FH CRC	221	17.7	1.32	5.4	NS
No exposure smoking	743	59.3	1.0	—	—
Low exposure smoking	326	22.6	0.90	N/A	NS
Heavy exposure smoking	226	18.0	1.90	13.9	.014

PAR-population attributable risk

**Results:** 2695 patients were screened. Men had a greater risk of significant neoplasia than for women (9.0% vs 6.9%;  $P = 0.037$ ). The  $P$  values for age refers to trend. Among women, BMI  $\geq 30$  had the highest PAR of all significant risk factors (see Table).

**Conclusion:** Our data suggest that BMI  $\geq 30$  is the most important risk factor for colorectal neoplasia in our asymptomatic women, accounting for up to 1 of 5 significant lesions detected on screening colonoscopy. Given the increasing number of obese patients in the US, identifying them as high risk may have important screening implications.

1221

**Strategies To Improve Scheduling and Completion of Screening Colonoscopy in a VA Setting**

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**Purpose:** Veterans Health Administration (VHA) directive mandates that screening colonoscopy must be completed < 60 days from referral. **Aim:** To determine the best scheduling strategy for implementation.

**Methods:** Three strategies were tested: primary care provider (PCP) generated an electronic (e-) consult to GI to schedule the patient (Group 1); or after discussion with patient, PCP generated an e-consult to GI AND each patient was given written information about screening colonoscopy and instructed to CALL GI "today" (Group 2); or COME TO GI "today" (Group 3) to schedule colonoscopy. One week after the e-consult, GI called the patients who did not initiate contact to schedule colonoscopy. Study period: 4/4/07–4/30/07. The following time intervals (days) were tabulated: e-consult to 1st GI contact, 1st GI contact to completed colonoscopy and e-consult to completed colonoscopy. Number of calls made by GI was recorded.

**Results:** 184 patients (37, 101 and 46 in Groups 1, 2 and 3) were referred. We excluded 10 who did not return phone calls after 3 messages; 12 who declined colonoscopy; 5 who had inappropriate referrals and 22 who were scheduled for colonoscopy after 6/4/07. The data of 135 patients were analyzed. Table 1 shows that when the scheduling was patient-driven (same day come to GI) time intervals were significantly shorter.

**Conclusion:** The strategy of having patients come to GI personally on the same day after PCP clinic visit resulted in significantly shorter time intervals compared to e-consult only and patient-initiated phone scheduling. This strategy also imposes the least amount of work load (initiating contact with patients) on GI as seen by the significantly smaller number of calls needed to schedule the patients. Patient-initiated same day personal scheduling with GI appears to be the most efficient and effective to ensure timely completion of screening colonoscopy.

1222

**A Paid Day Off from Work Increased Willingness To Have Screening Colonoscopy**

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**Purpose:** Screening rate for colorectal cancer is still low. In an effort to increase screening rates we conducted a survey among hospital employees to assess if a paid day off from work will increase rates of colon cancer screening.

**Methods:** All hospital employees of Bronx Lebanon Hospital Center, New York were given an anonymous questionnaire which was distributed through payroll. A pre-stamped envelope was provided so the questionnaire could be returned by mail.

**Results:** A total of 4501 surveys were distributed and 916 (20.4%) employees responded. More women than men returned the surveys (658 versus 258). Among those who responded 789 (86.1%) were aware of colon cancer screening, 384 (41.9%) were more than 50 years old and 161 (17.6%)

Intervals (days)	e-Consult Only N = 28	Patient Called GI N = 25	Patient Did not Call GI N = 46	Patient Came to GI N = 21	Patient Did not Come to GI N = 13
e-Consult to 1st GI Contact	9.9 + 3.5 $\pm$	4.5 + 3.2 $\pm$	12.6 + 5.6 $\pm$	0.5 + 1.1* $\pm$	10.9 + 4.8 $\pm$
1st GI Contact to Colonoscopy	18.8 + 3.4 $\pm$	19.2 + 3.2 $\pm$	19.3 + 2.6 $\pm$	14.2 + 2.9 $\pm$	12.5 + 2.2 $\pm$
e-Consult to Colonoscopy	28.6 + 3.5 $\pm$	23.7 + 3.4 $\pm$	31.9 + 2.8 $\pm$	14.7 + 3.0* $\pm$	23.5 + 3.1 $\pm$
Number of Calls Made by GI	1.5 + 0.1 $\pm$	1.3 + 0.1 $\pm$	1.8 + 0.1 $\pm$	0 + 0* $\pm$	1.8 + 0.3 $\pm$

\* vs all other,  $P < 0.05$ , ANOVA with contrasts

had family history of colon cancer or polyps. Among 161 respondents with family history of colon cancer or polyps, 11 (6.8%) were not aware of colon cancer screening tests, 78 (48.4%) were over the age of 50 and only 58 (36%) had a screening test for colon cancer. Of all the respondents, 297 (32.4%) had one or more of screening tests. Eighty nine of them had stool test for occult blood, 16 had barium enema, 27 had sigmoidoscopy and 235 had colonoscopy. Of 603 respondents who never had a screening test, 407 (67.5%) were willing to have a screening test, 101 were not sure, 90 (14.9%) were not willing to have a screening study and 5 did not respond to the question. Six hundred and ninety one (75.4%) of respondents were willing to have an initial or if needed a repeat screening colonoscopy if given a paid day off from work. Of 63 respondents who were above 50 years and not willing to have an initial or a repeat screening colonoscopy, 28 (44.4%) were willing to have colonoscopy if given a paid day off. Among 228 respondents who were unwilling to have an initial or a repeat screening colonoscopy, there was statistically significant difference between male and female respondents who finally would go for the screening colonoscopy if they were given a paid day off [61% (27/44) male versus 38.6% (71/184) female,  $P = 0.006$ ].

**Conclusion:** Our survey suggests that among health care employees who were initially unwilling to have screening colonoscopy, a paid day off from work may increase willingness to have the procedure. This was significantly higher in male respondents than female. A prospective study is needed to assess the effectiveness of this strategy.

## 1223

### CT Colonography (CTC) Reporting and Data System (CRADS): An Effective Method To Manage Extracolonic (EC) Findings

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**Purpose:** CT colonography (CTC) is a new technology used to visualize the colon and rectum. EC findings have raised concerns regarding additional expense, patient anxiety and morbidity. CTC Reporting and Data System (CRADS) is a classification system devised to help direct this work up. In this schema, E3 and E4 represent clinically significant findings requiring additional follow up. Most findings are E2 or clinically insignificant and require no follow up. This classification system guides the physician to avoid unnecessary work up of benign findings. Our study retrospectively investigates the impact of CRADS on the work up of patients with E2 findings.

**Methods:** We retrospectively reviewed all CTC reports from July 2003 to June 2006. CRADS was fully implemented at our institution on January 1, 2006. Prior to this date, no specific classification system was used for EC findings. For all CTC reports prior to January 1, 2006, a CRADS score was assigned retrospectively by a board certified radiologist. We compared the number of patients with E2 findings that received follow up pre and post CRADS implementation. Radiology studies generated from E2 findings pre and post CRADS implementation were also calculated.

**Results:** 2277 patients had CTC from July 2003 to June 2006. 1038 patients (45.6%) had a total of 2092 EC findings. E3 and E4 findings were found in 252 (11%) patients. E2 findings were found in 791 patients (34.7%). Within the E2 category, there were 555 patients with E2 findings prior to Jan 1, 2006 and 236 patients over the next 6 months. Demographics were similar. In patients with E2 findings, 9.2% (51/555) had follow up studies prior to implementation of CRADS and 4.7% (11/236) had follow up studies after CRADS implementation ( $P = 0.03$ ). There was also a significant difference ( $P = 0.0004$ ) in the total number of studies generated before (72 studies) and after (11 studies) January 1, 2006. There were no adverse outcomes from any of the E2 findings identified over this time period.

**Conclusion:** CRADS is an effective method to stratify EC findings. In this study, implementation of this system significantly decreased the number of follow up radiology studies ordered. CRADS reduces cost, patient anxiety and morbidity. No E2 findings were found to be malignant. This study validates CRADS as a tool to help primary care providers manage EC findings.

## 1224

### Comparing Adenoma Detection Rates among Colonoscopies Prepped by Bowel Lavage with Sodium Phosphate Solution vs Pegylated Electrolyte Lavage Solution

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**Purpose:** To compare adenoma detection rates (ADRs) between patients undergoing colonoscopy after colonic lavage with sodium phosphate solution vs a pegylated electrolyte lavage solution, and subsequently characterize the pathology based on degree of severity.

**Methods:** One thousand consecutive colonoscopies were studied for each bowel lavage group, with retrospective analysis to determine ADR and further characterize pathology. One group underwent pre-colonoscopy lavage with sodium phosphate solution and the other with a pegylated electrolyte lavage solution. All colonoscopies were performed by the same five endoscopists in one University practice group. Comparisons were made of colon cancer detection rates, and ADR with characterization of adenomas greater than or less than 1 cm. Statistical analysis included T test, Chi-square multivariate analysis and Odds ratios.

**Results:** Please see table below. Sodium phosphate lavage solution group = NaP. Pegylated electrolyte lavage solution group = PEG.

**Conclusion:** Bowel lavage preparation with sodium phosphate solution resulted in a significantly higher Adenoma Detection Rate and identified more patients overall with adenomas, compared to bowel lavage with a pegylated electrolyte lavage solution. However, there was no difference in the detection of significant pathology, as defined by adenomas >9 mm or neoplastic lesions. We feel that it is important to recognize that pegylated electrolyte lavage solutions perform as well as the sodium phosphate solutions in the detection of significant pathology, given the concerns regarding nephrotoxicity risks with sodium phosphate.

	NaP lavage (N = 1000)	PEG lavage (N = 1000)	
Total adenomas per 1000 colonoscopies	514	426	$P 0.03$
Total adenomas > 9 mm	74	79	$P 0.7$
Total adenomas < 10 mm	440	347	$P 0.01$ OR 1.3
Total Patients with any adenomas	308	257	$P 0.01$ OR 1.28
Patients with adenoma > 9 mm	62	61	NS
Patients with adenomas < 10 mm	266	215	$P 0.007$ OR 1.3
Cancers < 10 mm	4	1	NS
Cancers > 9 mm	8	3	NS

1225

**Yield of Screening Colonoscopy Performed 6–7 Years after a Negative Colonoscopy in a Veteran Population**

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**Purpose:** Colonoscopy is being increasingly used for colorectal cancer screening. Current guidelines based on limited data recommend a 10 year followup examination after a negative colonoscopy in average risk individuals. Concern has been raised, however, over reports of interval colon cancers detected less than 10 years after a negative colonoscopy. Data indicate that many individuals are being screened at a shorter interval. The goal of the present study was to examine the results of screening colonoscopy in patients with a prior negative colonoscopy at the VA Western New York Medical Center.

**Methods:** We retrospectively reviewed the electronic database of screening colonoscopies performed between 2003 and 2006. Patients who had a previous colonoscopy for screening or diagnostic purposes that did not show adenomatous polyps were identified. Pathology reports from the screening colonoscopy were reviewed. Advanced polyps were defined as those greater than or equal to 1 cm, with villous histology, or high grade dysplasia or cancer.

**Results:** A total of 1798 patients had screening colonoscopies during the study period. 138 patients had a prior negative colonoscopy; 41 (30%) had their initial colonoscopy done at the VA Western NY Medical Center. The second colonoscopy reached the cecum in 98%. 97 (70%) were average risk patients and 41 (30%) had a family history of colon cancer. In the average risk group, 26 (27%) patients had polyps, 10 (10%) had adenomas, and none had advanced adenomas; the second colonoscopy was done at an average of 7 years after the initial examination. Of those with positive family histories, 11 (27%) patients had polyps, 3 (7%) had adenomas, and one patient had an advanced polyp (1 cm) in the proximal colon; the second colonoscopy was done at an average of 6 years after the initial examination. There was no difference in the incidence of adenomas between average risk patients and those with a positive family history. No colorectal cancers were found in either group.

**Conclusion:** In this patient population, a second colonoscopy performed at an interval of 6–7 years, had a low yield of adenomas and advanced adenomas. Therefore, a screening interval of 10 years after an initial negative examination appears reasonable.

1226

**Should Colonoscopy Withdrawal Time Recommendations Be Adjusted for Patient or Procedure Factors?**

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**Purpose:** The ACG/ASGE Quality Taskforce recommended a mean colonoscopy withdrawal time  $\geq 6$  minutes for normal screening colonoscopies to maximize polyp detection; however, this recommendation may need adjustment for patient- or procedure-related factors.

**Methods:** To determine if there are patient- or procedure-related characteristics associated with colonoscopy withdrawal time, we prospectively collected data from patients presenting for screening colonoscopy at an urban academic medical center. Patient demographic information, colonoscopy withdrawal time and bowel preparation quality were collected. Withdrawal time was the interval between initiation of withdrawal in the cecum and removal of the colonoscope from the patient. We excluded patients with polyps. We used the Wilcoxon rank-sum test and Pearson's correlation coefficient to assess for associations between colonoscopy withdrawal time and potential predictor variables, including age, gender, race (Caucasian vs. non-Caucasian), marital status (married vs. non-married), primary language

(English vs. non-English), history of prior colonoscopy, and quality of bowel preparation (excellent/good/fair vs. poor/unsatisfactory).

**Results:** There were 362 screening colonoscopies with withdrawal times documented. Exclusion of 139 cases with polyps left 223 procedures for analysis. There were 85 men (38%) and the median age was 56 (interquartile range [IQR] 51–62). Thirty-nine (17%) were Caucasian, 77 (35%) were married, 141 (63%) were English-speakers, and 50 (22%) had a prior colonoscopy. Bowel preparation was considered poor or unsatisfactory in 10 (4%) cases. The median colonoscopy withdrawal time was 6 minutes (IQR 5–8 minutes). There were no significant associations detected between any variables and withdrawal time, including age ( $P = 0.35$ ), race ( $P = 0.64$ ), marital status ( $P = 0.63$ ), language ( $P = 0.40$ ), history of prior colonoscopy ( $P = 0.91$ ), or poor/unsatisfactory bowel preparation ( $P = 0.45$ ). The median colonoscopy withdrawal time for both men and women was 6 minutes, but the IQR was larger for men (5–9 vs. 5–8 minutes), resulting in a trend toward significance ( $P = 0.08$ ).

**Conclusion:** The use of a single value to define an “appropriate” colonoscopy withdrawal time appears justified for a broad range of patients regardless of factors such as age and race. Future studies should confirm that gender-specific withdrawal time recommendations are not necessary.

1227

**Measuring Compliance with Routine Screening Recommendations in Health Care Workers**

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**Purpose:** Colorectal cancer is the third most commonly diagnosed cancer in men and women in the United States. However, most Americans are not screened for colorectal cancer. Information from the National Health Interview Survey indicates that in 1992, only 17.3% of people 50 years of age or older had undergone fecal occult blood testing in the previous year, and 9.4% had undergone sigmoidoscopy in the previous 3 years.

As screening reduces mortality, the aim of this study was to determine compliance with routine health screening recommendations among health care workers.

**Methods:** A 1 page questionnaire distributed to health care workers within the United Health Services, which were color coded to differentiate various health care professions such as doctors, nurses, and other health care staff were sent out anonymously from September 2006 to December 2006. The main outcome measure was to determine the recent use of Colonoscopy, but cancer preventive interventions like Papanicolaou (Pap smear) and Pelvic

All Job Classifications				
	Screening eligible	Compliant	Non-compliant	%
Mammogram	45	41	4	91.1%
Colonoscopy	73	57	16	78.1%
PSA/DRE	68	46	22	67.6%
Pap smear and Pelvic Exam	70	62	8	88.6%
Physicians				
	Screening eligible	Compliant	Non-compliant	%
Mammogram	15	11	4	73.3%
Colonoscopy	52	43	9	82.7%
PSA/DRE	63	41	22	65.1%
Pap Smear and Pelvic Exam	4	4	0	100%

Exam, Mammography, PSA level testing or Digital Rectal Exam of the prostate gland were also included.

Health care workers across the ages of 19 to 61 were assessed for compliance with screening recommendations that were valid for their age and gender.

**Results:** A total of 169 surveys were found to be valid. The compliance rate with colonoscopy for physicians was 82.7% compared with the other job classifications of 78.1%. The results were interpreted according to the guidelines approved by the American Cancer Society between Physicians and All Job Classifications that included nurses, pharmacists, non clinical and ancillary staff.

**Conclusion:** The results from the study reflect the need to continue efforts to raise awareness regarding screening preventable cancers notably colorectal cancer.

## 1228

### Marked Racial/Ethnic Differences in Acceptance of and Barriers to Colorectal Cancer Screening in a Primary Care Setting

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**Purpose:** Racial/ethnic minorities have an increased incidence of colorectal cancer (CRC) and tend to present with a more advanced stage of CRC relative to whites. In addition, studies have shown that racial/ethnic minorities are also less likely to undergo CRC screening tests (including fecal occult blood testing [FOBT], flexible sigmoidoscopy [FS], and colonoscopy) than whites. The aim of this study was to identify the proportion of racial/ethnic minorities that are offered and accept CRC screening and to identify barriers to CRC screening among racial/ethnic minorities over the age of 50 years as compared with whites.

**Methods:** Subjects  $\geq 50$  years old completed a detailed questionnaire at the time of their scheduled outpatient primary care clinic visit. Data collected included demographics, self-reported race/ethnicity, prior CRC screening (FOBT, FS, and/or colonoscopy), as well as barriers to CRC screening.

**Results:** Of the 688 subjects enrolled, 376 were white (W), 188 were black (B), 92 were Hispanic (H), and 32 identified their race/ethnicity as other (O). W patients were slightly older than B, H, or O racial/ethnic groups (65.0 vs. 62.1 vs. 62.5 vs. 63.7 years;  $P = 0.002$ ) but had a similar prevalence of male subjects (93.1% vs. 92.0% vs. 91.3% vs. 81.3%,  $P = 0.13$ ). There were no significant differences between W, B, H, and O racial/ethnic groups who were offered FOBT (73.7% vs. 73.9% vs. 69.6% vs. 59.4%;  $P = 0.31$ ), FS (60.4% vs. 52.1% vs. 51.1% vs. 56.3%;  $P = 0.18$ ), or screening colonoscopy (73.7% vs. 67.0% vs. 67.4% vs. 68.8%;  $P = 0.34$ ). However, whites were significantly more likely than racial/ethnic minorities to ever have completed FOBT (71.0% vs. 59.6% vs. 48.9% vs. 28.1%;  $P < 0.001$ ), FS (60.4% vs. 49.5% vs. 34.8% vs. 28.1%;  $P < 0.001$ ), and screening colonoscopy (73.1% vs. 49.5% vs. 43.5% vs. 53.1%;  $P < 0.001$ ). In addition, we found that there were significant differences in the number and type of barriers to CRC screening between whites and racial/ethnic minorities.

**Conclusion:** Racial/ethnic minorities are less likely to undergo CRC screening than whites. The lower rate of CRC screening among racial/ethnic minorities is not due to provider discrimination and is explained by a lower acceptance rate among racial/ethnic minorities as compared with whites. Future studies to attempt to overcome barriers to CRC screening among racial/ethnic minorities are needed.

## 1229

### Gastroenterologists' Patient Instructions for Oral Sodium Phosphate Solution for Colonoscopy Preparation: A Survey among Gastroenterologists in the State of Indiana

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**Purpose:** Oral sodium phosphate solution (OSPS) has been associated with acute renal failure when used as a bowel preparation for colonoscopy. Our aim was to determine whether gastroenterologists in Indiana follow recent recommendations for safe and effective use of colonoscopy.

**Methods:** The study, conducted from May to September 2006, included practicing gastroenterologists in Indiana. Our office reviewed each physician's written instructions on the use of OSPS for bowel preparation with respect to dosages, timing of dose, hydration instructions and type of hydration solution recommended to patients receiving OSPS. These were compared to safety recommendations developed by American Society of Colon and Rectal Surgeons, The American Society of Endoscopy and The Society of American Gastrointestinal and Endoscopic Surgeons which included use of no more than two 45 ml bottles given at least 6–12 hours apart, approximately 960 ml of fluid given with each dose of OSPS and preference given to carbohydrate-electrolyte solutions. Descriptive statistics was used for our data analysis.

**Results:** 193 (97.5%) physicians participated in the study. 80.3% used OSPS in their practice, with a mean total amount of solution given 87.3 ml. There were no physicians that recommended more than 90 ml of OSPS. The mean interval recommended between doses was 7.6 hours. 35.5% physicians prescribed two 45 ml bottles of OSPS at an interval less than six hours apart. 9.7% of physicians using OSPS specified the amount and type of fluid prior to first dose of OSPS, with a mean (range) of 660 ml (120–1440 ml). 93.7% of physicians specified the fluid amount to be taken with or after the first dose of OSPS with a mean (range) of 1002 ml (120–3000) ml. 89% of physicians specified an amount of fluid to be taken with and after the second dose of OSPS with a mean (range) of 660 ml (120–1560 ml). Carbohydrate rich solution was preferred by 22% of physicians after the first and 16% of physicians after the second dose. 33.5% physicians using OSPS recommended more than 1920 ml of fluid to be taken with the OSPS prep.

**Conclusion:** Practicing Indiana gastroenterologists were universally consistent with recent guidelines in their written instructions to patients with regard to the total dose of OSPS for colonoscopy. They frequently recommended OSPS at intervals shorter than current guidelines and often did not give optimal instructions with regard to hydration during colonoscopy.

## 1230

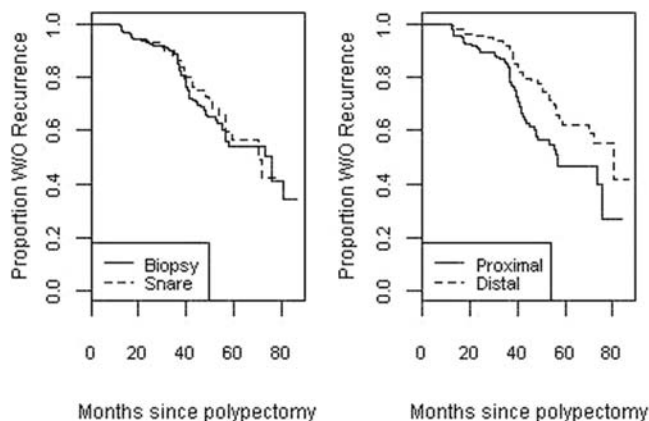
### Location of Adenoma, Not Removal Method, Is Associated with Recurrent Neoplasia

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**Purpose:** Certain adenoma characteristics such as size  $\geq 10$  mm, multiplicity ( $>2$ ) and advanced histology are associated with recurrent neoplasia. The effect of method of polypectomy or location of polypectomy on recurrent neoplasia has been less widely studied. We analyzed the effect of different polypectomy methods (hot and cold biopsy [BX] vs hot and cold snare [SN]) and location of polyp removed, proximal vs distal, on polyp recurrence.

**Methods:** Colonoscopy and medical records of all individuals who had 1 polyp removed from a single colon segment and a FU colonoscopy  $\geq 12$  mos after polypectomy were included. Polyp size, morphology, pathology and location, method of polypectomy were included. Univariable and multivariable Cox proportional hazards models were used to estimate the hazard rates for polyp recurrence. Recurrence defined as a polyp detected on FU in the same segment as initial polypectomy. "Proximal" defined as cecum, ascending and transverse colon and "distal" as descending, sigmoid and rectum.

**Results:** 385 subjects (551 polyps) with a mean age of 62 yrs (62% male) were included. Polyps recurred in 23%. Recurrence was associated with polyp location: 28% in right vs 18% in left colon ( $P < 0.001$ ) but not polypectomy method 23% that had BX vs 21% that had SN ( $P = 0.6$ ). [figure 1] Even after adjusting for age, polyp size and location, polypectomy type is not associated with polyp recurrence. Contrarily, after adjusting for age, polyp size and polypectomy type, the location of polypectomy was significantly associated with polyp recurrence.



\*Recurrence after Polypectomy

Factor	Level	HR (95% CI)	P value
Polypectomy	BX vs SN	1.2 (0.74–1.9)	0.48
Polyp Location	Proximal vs Distal	1.8 (1.3–2.7)	0.001
Polyp Size	1 level increase (ie 6–9 vs 1–5, etc)	1.3 (1.01–1.8)	0.042
Age	5 yr increase	1.1 (1.03–1.2)	0.007

Cox proportional hazards multivariable analysis

**Conclusion:** The use of BX is not associated with an increased risk of polyp recurrence. Most surprising was the significant association found between polyps removed from the right side of the colon and an 80% risk of polyp recurrence in that segment on FU.

## 1231

**Colon Cancer Screening at an HIV Outpatient Clinic: 2000–2006**

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**Purpose:** It is currently unknown if patients with HIV have an increased risk of colon cancer in the era of highly active anti-retroviral therapy (HAART). Since patients with HIV are living longer, routine primary care and cancer screening is recommended. It has previously been reported that colon cancer screening is underutilized in the HIV population. We sought to determine, over 6 years, the frequency and selected modality of colon cancer screening in patients with HIV who were at least age 50 and were being followed at a comprehensive HIV clinic in downtown Atlanta between 2000 and 2006.

**Methods:** We obtained a randomized sample of 81 out of 849 patients with HIV who were age 50 or older and who were seen at the HIV clinic on Ponce de Leon Avenue in downtown Atlanta, Georgia between 2000 and 2006. From the medical charts, we obtained information on age, gender, presence of colon cancer screening, selected modality of colon cancer screening, CD4 count and viral load closest to the time of screening, and use of HAART.

**Results:** Of the 81 patients sampled, 23 (28.4%) did not undergo any colon cancer screening test during the specified time period. 31 patients (38.3%) underwent fecal occult blood testing (FOBT), but not every year. 20 patients (25%) underwent a combination of FOBT and lower endoscopy (12 had a colonoscopy and 8 had a flexible sigmoidoscopy). 6 patients (7.4%) underwent colonoscopy alone, and one patient (1.2%) underwent flexible sigmoidoscopy alone. Six patients refused colonoscopy (two of them under-

went FOBT). The majority (69%) of patients were male. The majority of patients were taking anti-retrovirals at the time of screening.

**Conclusion:** In the post-HAART era, the majority of patients who were age 50 or older and seen in this comprehensive HIV clinic in Atlanta underwent some form of colon cancer screening. FOBT testing was utilized most often (63% of patients) but was not performed on a strict yearly basis. 22% of patients underwent colonoscopy and 11% of patients underwent flexible sigmoidoscopy. When compared to data from the general population regarding colon cancer screening, patients with HIV in this study were more likely to undergo FOBT or flexible sigmoidoscopy and less likely to undergo colonoscopy. More data is needed to investigate the risk of CRC with HIV in the era of HAART.

## 1232

**Endoscopists Recommend Shortened Surveillance Intervals**

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**Purpose:** In 2006 the American Cancer Society and US Multi-Society Task Force on Colorectal Cancer published consensus guidelines for surveillance colonoscopy after colorectal cancer and polyps. Dissemination and implementation of guidelines may lag in practice. We queried endoscopists who use CORI on knowledge of guidelines and practice recommendations, and will later compare to practice in the National Endoscopic Database (NED). We analyzed endoscopist recommendations for common scenarios as compared to guidelines, and for characteristics associated with variance.

**Methods:** All endoscopists who contribute data to NED were invited to complete a survey via secure applet, mail, fax or telephone. Responses to the survey were stored confidentially. Survey questions were directed at endoscopist demographics and practice description. We constructed seven patient scenarios to test knowledge of guidelines in cases of tubular adenomas, tubulovillous adenomas, hyperplastic polyps, personal history of colorectal cancer (CRC) and family history of CRC.

**Results:** Overall, 287 of 442 (65%) endoscopists participated, with 71% among 356 practicing endoscopists and 38% in 86 fellows responding. Respondents were primarily male (86%), Caucasian (74%, 21% Asian) gastroenterologists (90%) with a mean age of 45 years. Respondents complete 50–2,000 colonoscopies annually, with a mean of 676 procedures. The most influential factor for colorectal cancer and polyp surveillance was cited as clinical evidence in literature (89% rated very significant).

Each clinical scenario revealed endoscopists would recommend a surveillance interval shorter than the guidelines. Those most likely to recommend shorter intervals for 1–2 small adenomas are non-gastroenterologists (46% v. 15%,  $P < 0.0001$ ) and endoscopists not very influenced by clinical evidence (45% v. 15%,  $P < 0.0001$ ), nor by US Multi-Society Task Force (27% v. 8%,  $P < 0.0001$ ). Shortened intervals for hyperplastic polyps are seen in non-gastroenterologists (54% v. 22%,  $P < 0.001$ ).

**Conclusion:** A significant proportion of endoscopists suggest surveillance colonoscopies for low-risk patients at more frequent intervals than recommended. This could have a profound effect on endoscopy workforce demands and limit availability for screening colonoscopy.

## Proportion recommend shorter interval

Scenario	Published interval (years)	Proportion surveillance shorter than guideline
Small tubular adenoma	5	18%
Multiple small adenomas	3	7%
Large adenoma	3	12%
Villous adenoma	3	17%
Hyperplastic polyps	10	25%
Personal history CRC	3	22%
Family history CRC	5	14%



1233

### An Elevated Rate of Adenoma Detection in an Urban Latin American Population Undergoing Colorectal Cancer Screening

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**Purpose:** Colorectal cancer is the second leading cause of cancer death in the United States. African Americans (AA) are known to have an elevated rate of colonic neoplasms compared to the general population. There is limited data on Latin Americans (LA) undergoing screening colonoscopies with respect to the incidence and location of neoplasms. We retrospectively reviewed screening colonoscopies performed at an inner city university hospital that serves a predominately minority population to detail colon polyp size, distribution, and pathology with respect to ethnicity.

**Methods:** There were a total of 2,698 colonoscopies performed at the University Hospital in Newark, NJ from 2005–2006. Of these, 756 were screening colonoscopies performed on patients who were asymptomatic. These cases were analyzed for presence, location, size, and pathology of polyps with respect to patient ethnicity.

**Results:** Of the 756 screening colonoscopies, 287 (38%) were performed in LA and 331 (44%) in AA. In LA, 112 patients (39%) were found to have at least one polyp. This was not significantly different from AA (145 patients; 44%). Additionally, 56 (19%) LA were found to have a right-sided lesion (proximal to the splenic flexure), which was comparable to AA (64 patients; 19%). Significant pathology was defined as adenomatous change (AD), tubular adenoma (TA), tubulovillous adenoma (TVA), villous adenoma, or carcinoma (CA). Of the AA patients screened, 67 (46%) had pathologically significant lesions (5 AD, 53 TA, 6 TVA, and 3 CA). LA had a similar incidence (54 patients; 48%) and distribution of pathologically significant lesions (2 AD, 47 TA, 5 TVA, 0 CA). The percentage of pathologically significant right-sided polyps were similar in AA (40 patients, 62%) and LA (32 patients, 57%). Of note, AA were significantly more likely to have a large (> 1 cm) polyp than LA (8.5% vs. 3.1%,  $P < .01$ ), and were more likely to have a large right sided colonic polyp (4.6% vs. 1.7%,  $P = .07$ ).

**Conclusion:** This study provides evidence that LA undergoing screening colonoscopy have a higher than expected incidence of colonic polyps, pathologically significant lesions, and pathologically significant right-sided lesions. These findings were similar to those of AA, a known high-risk group. Our study suggests that screening guidelines for LA should reflect those for AA and warrants further prospective trials.

1234

### Mechanisms of Polyethylene Glycol (PEG) Anti-Proliferative Effects: Implications for Colon Cancer Chemoprevention

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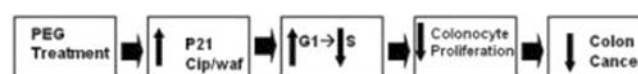
**Purpose:** The recent high profile failure in clinical trials of agents such as folate (*JAMA* 2007) and celecoxib (*NEJM* 2006) have underscored the urgency of developing safer and more effective chemopreventive agents against colon cancer. One of the most promising agents in preclinical studies is PEG, a widely used OTC agent for chronic constipation. However, progress developing this agent has been stymied by lack of mechanistic insights. We have reported that PEG markedly suppressed epithelial hyperproliferation (Roy et al., *Mol Cancer Ther* 2006). The present study explores the molecular mechanisms of this effect.

**Methods:** The human colon cancer cell line HT-29 was used for these studies. Cells were treated with 10% PEG 8000 or vehicle for 24 hours. Proliferation was assessed by expression of proliferating cell nuclear antigen (PCNA). Cell cycle distribution was assessed by flow cytometry using propidium

iodide. Immunoblot analysis with densitometry was performed with standard techniques.

**Results:** 10% PEG 8000 treatment decreased PCNA expression (74.9% of control,  $P < 0.01$ ) indicating an anti-proliferative effect. PEG markedly increased in proportion of non-replicating cells (G0-G1 phase  $82.6 \pm 1.1\%$  vs  $51.6 \pm 4.1\%$  in vehicle controls,  $P < 0.005$ ) with a concomitant profound suppression of cells undergoing DNA replication (S phase  $11.7 \pm 6.3\%$  vs  $44.9 \pm 4.5\%$  in controls,  $P < 0.005$ ) indicating a G1-S phase arrest. The effect on cell cycle with PEG 3350 was intermediate between control and PEG 8000 (S phase ~36%) consistent with *in vivo* data (Roy et al., *Cancer Lett* 2004). To assess the mechanisms, we evaluated p21 cip/waf, a potent inhibitor G1/S phase transition, which is frequently lost during colon carcinogenesis. We observed that PEG dramatically augmented p21 cip/waf expression (322% of control,  $P < 0.0001$ ).

**Conclusion:** We demonstrate, for the first time, that the chemopreventive properties of PEG may be related to induction of the tumor suppressor gene p21 cip/waf with concomitant G1/S phase cell cycle arrest (see figure). This provides biological rationale and an intermediate biomarker for the planned clinical chemoprevention trials with PEG.[figure1]



1235

### Gender and Subsite Locations Modulate the Chemopreventive Efficacy of Celecoxib: A MIN Mouse Study

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**Purpose:** Elucidating determinants of chemopreventive responsiveness is of major importance in designing cost-effective strategies against colorectal cancer (CRC) given the profound biological differences in the proximal and distal colon. Our group and others have demonstrated that gender impacts upon CRC location (*Arch Int Med* 2006). However, no previous studies have addressed the effects of gender on efficacy of chemopreventive agents against colonic neoplasia. We, therefore, conducted a study with the well-validated murine model of FAP, the MIN mouse, using a potent, well-established chemopreventive agent, celecoxib.

**Methods:** Male (N = 39) and female (N = 32) MIN mice, 5–6 weeks old, were assigned to either AIN 76a diet alone or supplemented with celecoxib 1500 ppm. After ~10 weeks on diet, animals were euthanized and tumors scored by 3 independent observers blinded to treatment group. Separate counts from proximal small bowel (PSB), distal small bowel (DSB) and colon were recorded. A subset of tumors was histologically analyzed to confirm adenomas.

**Results:** Females were noted to have dramatically more polyps than males ( $52.3 \pm 13.9$  versus  $35.4 \pm 16.1$ ,  $P < 0.0005$ ). Celecoxib treatment resulted in a significant reduction in total polyp number ( $43.9 \pm 17.1$  to  $10.6 \pm 6.3$ ,  $P < 0.00001$ ), although the effect size was considerably greater in females than males ( $87.8\%$  versus  $63.8\%$ ,  $P < 0.001$ ). With regards to regional distribution, most adenomas were located in the DSB. Therefore, from a polyp number point of view, the largest reduction occurred there ( $34.0$  in females and  $16.2$  in males,  $P = 0.01$  for gender difference). However, the greatest relative decrease was found in the PSB where females experienced a remarkable 98.2% suppression in polyps whereas males had a 74.5% reduction. Intriguingly, in the colon, celecoxib did not afford males any protection ( $102.3\%$  of control,  $P = 0.93$ ) and actually promoted tumorigenesis in females ( $216.1\%$  of control,  $P < 0.05$ ).

**Conclusion:** We demonstrate, for the first time, that in the MIN mouse, that the chemopreventive agent celecoxib was substantially more effective

in females than males. Moreover, the adenoma suppression appeared to be determined, at least in part, by region of the intestine. Aside from providing important insights regarding the MIN mouse model, our study underscores the need to consider both gender and subsite differences in designing and analyzing chemoprevention trials.

## 1236

# Positive Predictive Value of Fecal Occult Blood Testing in Patients Taking Aspirin, Other NSAIDs, Warfarin or Clopidogrel

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**Purpose:** To compare the positive predictive value (PPV) of FOBT to detect advanced adenoma or advanced neoplasia in patients on anticoagulant or antiplatelet medication with those not on these medications (control group).

**Methods:** All patients that underwent a colonoscopy at our institution from 2/1/99 to 8/9/06 for positive FOBT (using Hemoccult II) were identified using a computer database. Medical records were reviewed, and patients were stratified into 5 groups a priori: aspirin users, other non-steroidal anti-inflammatory (NSAIDs) users, warfarin users, clopidogrel users, and controls. Primary outcome was the prevalence of advanced adenoma (AA—defined by presence of adenoma  $\geq 10$  mm or tubulovillous adenoma) or advanced neoplasia (AN—defined by presence of cancer, cancerous polyp, or high grade dysplasia).

**Results:** During the study period, 1126 patients underwent colonoscopy for a positive FOBT and met entry criteria. The average age of study participants was 69 years, and most were men. The PPV of FOBT for advanced colon neoplasia was significantly higher in the control group [30.5%] when compared with those on aspirin [20.5%;  $P = 0.003$ ], other NSAIDs [19.7%;  $P = 0.003$ ], clopidogrel [7.3%;  $P = 0.002$ ] or warfarin [20%;  $P = 0.05$ ]. The PPV of FOBT was significantly lower for those on clopidogrel than those on aspirin [ $P = 0.04$ ] or other NSAIDs [ $P = 0.05$ ], but not warfarin [ $P = 0.08$ ]. The PPV for FOBT was similar for those on aspirin, other NSAIDs and warfarin. There was a linear trend between the number of positive FOBT cards and prevalence of advanced colon neoplasia [ $P = 0.01$ ].

**Conclusion:** Anticoagulants and antiplatelet medications lower the PPV of FOBT for advanced colonic neoplasia. If feasible, these medications should be stopped prior to stool collection. If these medications cannot be safely stopped, other colon cancer screening modalities should be considered.[figure1]

